Cu-Catalyzed Oxidative Imino Diels-Alder Cyclization: Synthesis of Dihydrofuroquinolines

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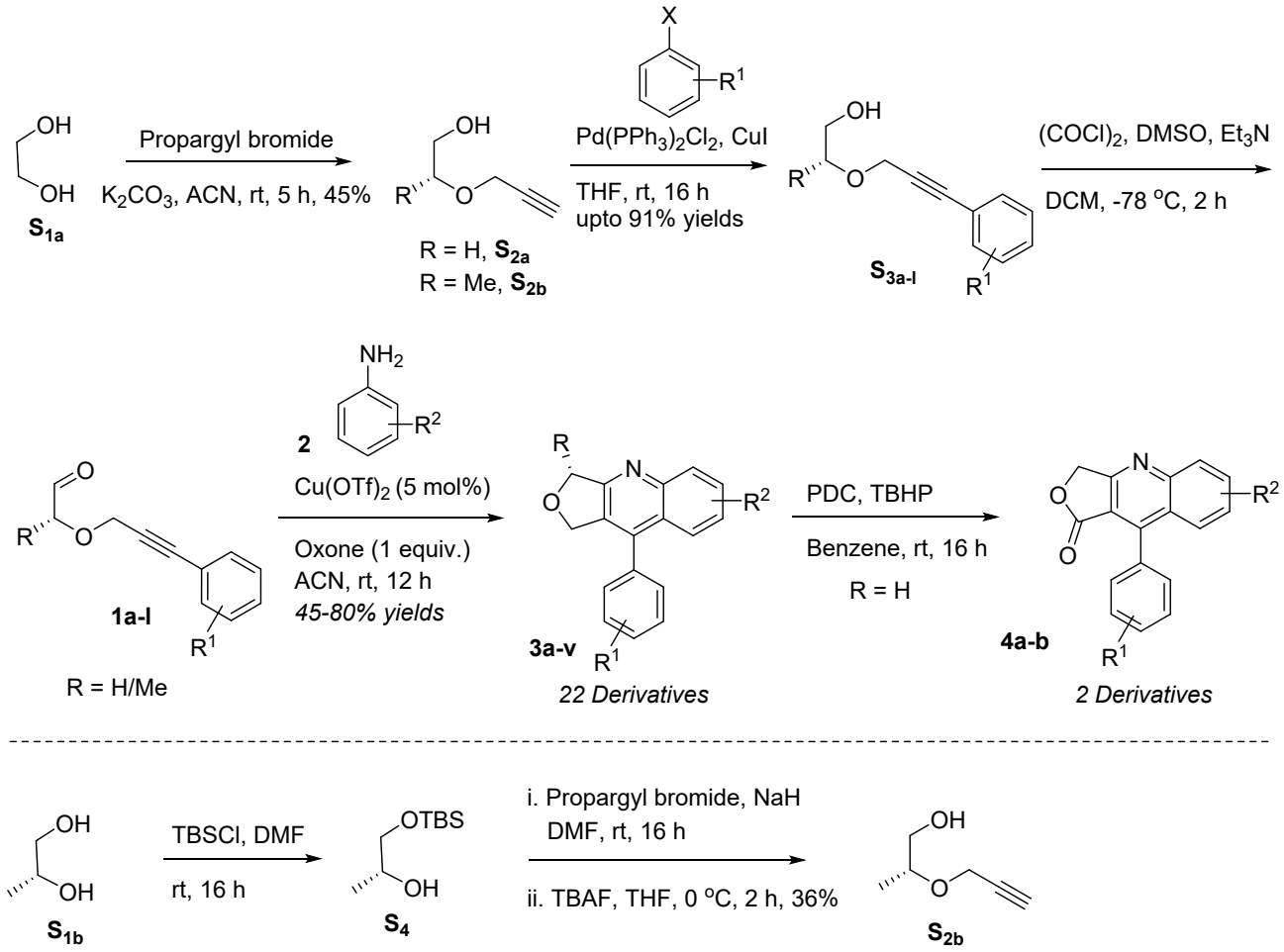
EXPERIMENTAL SECTION

General Methods:

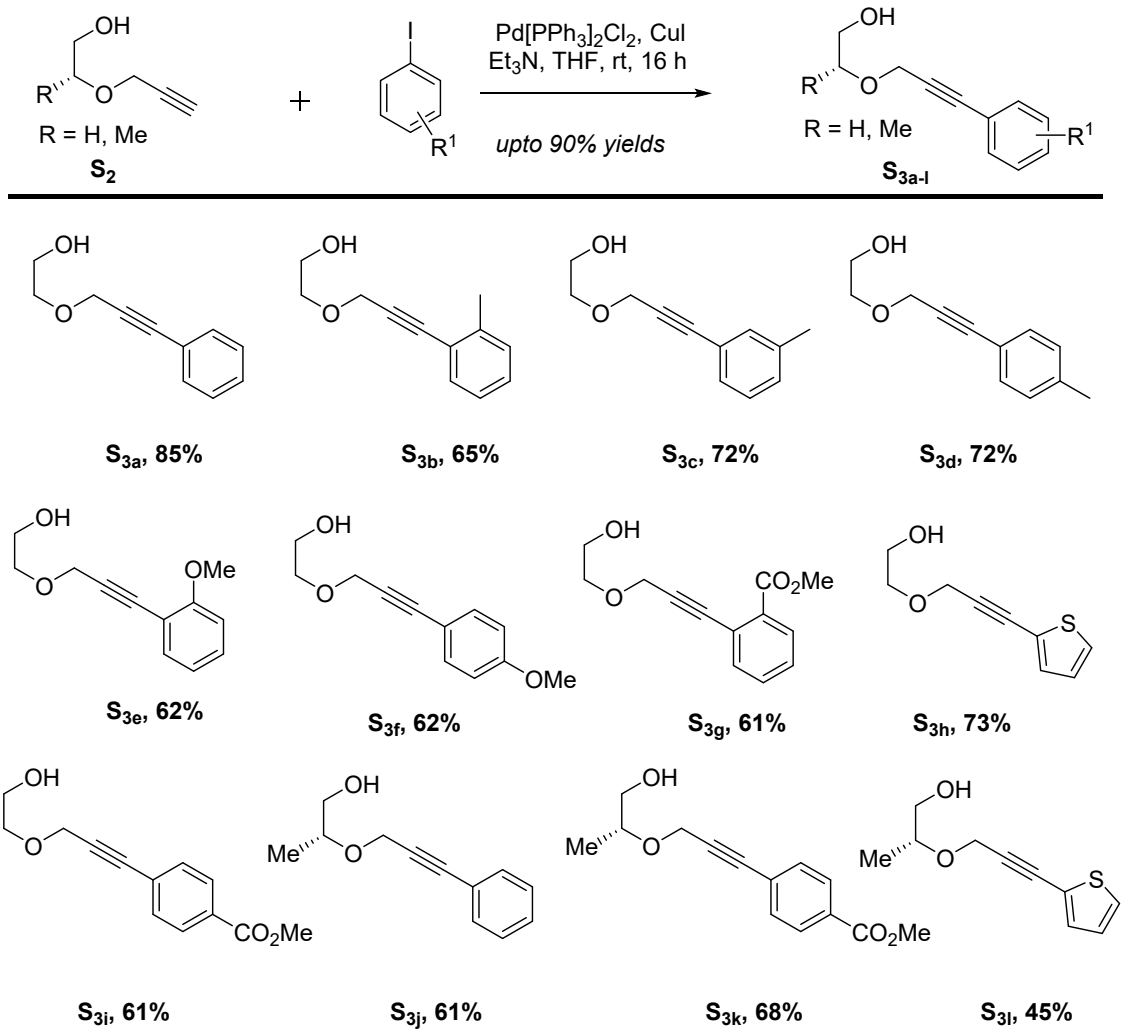
All reactions were carried out in flame-dried glassware under a Nitrogen atmosphere. Thin layer chromatography (TLC) was carried out on aluminium sheets coated with silica gel (60–120 and 100-200 mesh), and the spots were visualized with UV light at 254 nm or alternatively by staining with aqueous basic potassium permanganate or ceric ammonium molybdate. Column chromatography was performed on silica gel (60–120 and 100-200 mesh) using hexanes and ethyl acetate. Commercially available reagents were used as supplied and some of them were distilled before use. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ solvent on, 400 MHz and 500 MHz and 600 MHz NMR spectrometer (Chemical shifts were reported in ppm from tetramethylsilane with the solvent resonance as the internal standard in $CDCl_3$ solution, unless otherwise noted). Chemical shifts δ and coupling constants J are given in ppm (parts per million) and Hz (hertz) respectively. Chemical shifts are reported relative to residual solvent as an internal standard for ^{1}H and ^{13}C ($CDCl_3$: δ 7.26 ppm for ^{1}H and 77.0 ppm for ^{13}C). High resolution mass spectra (HRMS) [ESI+] were obtain using either a TOF or a double focusing spectrometer. ACN, DCM, THF and MeOH were dried immediately prior to use according to standard procedures. Acetonitrile, Dichloromethane was distilled under N_2 from CaH_2. All solvents were removed by evaporation under reduced pressure. Single-crystal X-ray diffraction data were collected on a Rigaku XtaLAB Synergy-I diffractometer using *CrysAlisPro* software, with graphite-monochromated Mo Kα (λ = 0.71073 Å) and Cu Kα (λ = 1.54184 Å) radiation at 293 K. The crystal structures were solved using the SHELXL-97 program implemented in OLEX2.0, and refined by full-matrix least-squares procedures on F^2. Anisotropic displacement parameters were applied to all non-hydrogen atoms Hydrogen atoms were placed in calculated positions and refined using a riding model with idealized geometries. Structural visualization and analysis were carried out using Mercury software for Windows.

Synthesis scheme for Dihydrofuroquinolines



Scheme S1: Synthetic strategy for the development of the methodology.

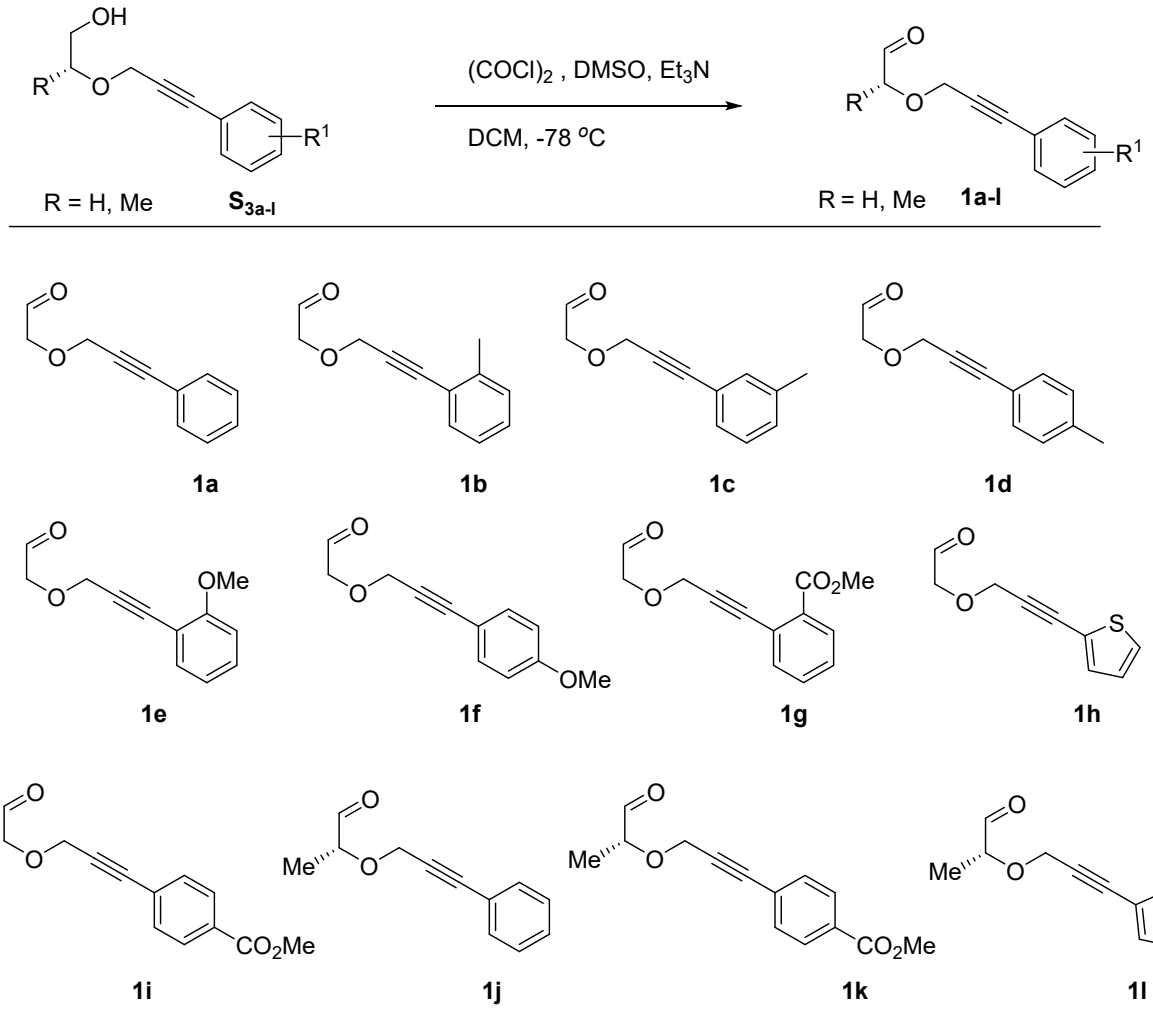
Synthesis Scheme of Sonogashira (S_{3a-l})



Scheme S2: List of Sonagashira cross coupled products prepared.

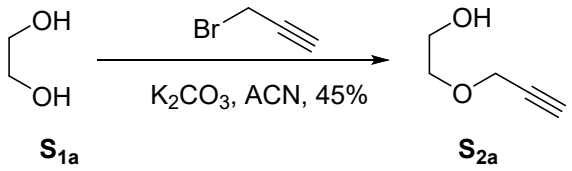
The experimental and spectral data of compounds **S_3**-**S_3h**, and **S_{3i}** is reported in previous reports.[1]

Synthesis Scheme of Aldehyde (1a-1l)



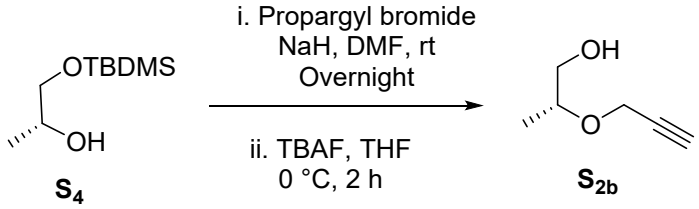
Scheme S3: List of aldehyde products synthesized.

General procedure A, for the synthesis of compound S_2 from S_1.



A stirred solution of diol **S_{1a}** (1 equiv.) in acetonitrile was treated with potassium carbonate (5 equiv.), followed by the careful dropwise addition of propargyl bromide (1.5 equiv.). Then the reaction mixture was stirred at room temperature for 5 h. After completion (monitored by TLC), the mixture was filtered through a celite pad. Next, 50 ml of water is introduced to the reaction mixture, which was then extracted with ethyl acetate three times (3 × 50 ml). The combined organic extracts are washed with brine (50 ml), dried over sodium sulfate, and concentrated under reduced pressure. Finally, the crude product is purified by flash column chromatography, resulting in Compound **S_{2a}** with considerable yield (up to 45%).

Synthesis of (*R*)-2-(prop-2-yn-1-yloxy)propan-1-ol (S_{2b}).

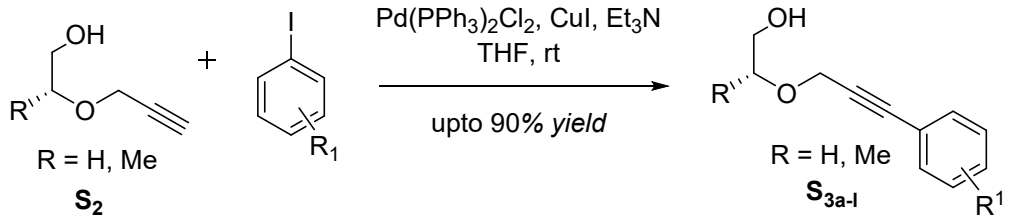


Step 1: A stirred solution of (*R*)-1-(*tert*-butyldimethylsilyl)propan-2-ol **S_4** (20.0 g, 1 equiv.) in anhydrous DMF at 0 °C under nitrogen was treated with sodium hydride (60% dispersion in mineral oil, 3.3 g, 1.2 equiv.) portion wise. After stirring for 30 minutes, propargyl bromide (1.2 equiv., 80 wt% solution in toluene) was added dropwise. The mixture was warmed to room temperature and stirred until complete consumption of the starting material, as confirmed by TLC. The reaction was quenched with saturated aqueous ammonium chloride, diluted with ethyl acetate, and the layers were separated. The organic extracts were washed with brine, dried over sodium sulfate, filtered, and concentrated. This crude product was directly used in the next step without purification.

Step 2: The above crude silyl-protected propargyl ether was dissolved in THF and TBAF (1.0 M solution in THF, 1.2 equiv.) was added dropwise at 0 °C and stirred for 1 hour until deprotection was confirmed by TLC. After quenching with aqueous ammonium chloride and extraction with ethyl acetate, the organic layers were washed, dried, filtered, and concentrated to yield (*R*)-2-(prop-2-yn-1-yloxy)propan-1-ol **S_{2b}** (4.7 g) as a yellow oil in 36% overall yield (over two steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.26 (dd, *J* = 15.8, 2.4 Hz, 1H), 4.21 – 4.12 (m, 1H), 3.81 – 3.72 (m, 1H), 3.65 – 3.57 (m, 1H), 3.51 – 3.45 (m, 1H), 1.14 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 80.15, 75.57, 74.35, 66.32, 56.22, 15.63.

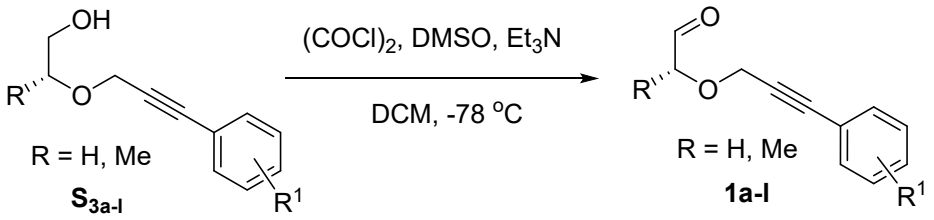
Note: Compound **S_4** was synthesized by using previous report.[2]

General Procedure B, for the synthesis of compounds S_{3a-l} from S_2.



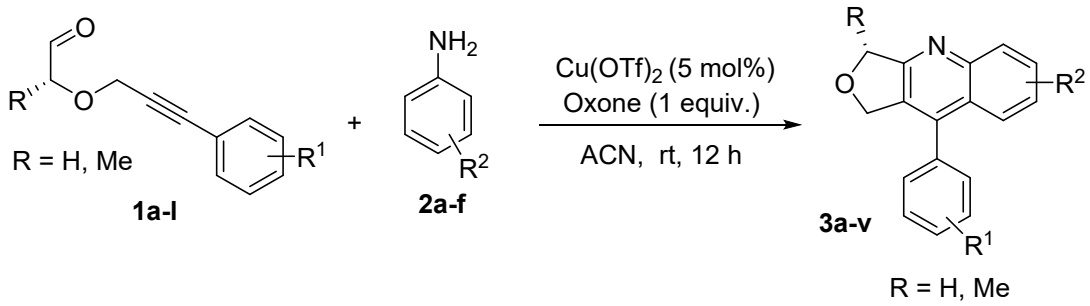
The stirred solution of compound **S_2** (1 equiv.) in THF (2 mL) was effectively reacted with a variety of substituted iodobenzene derivatives (1.1 equiv.), along with Pd $(PPh_3)_2Cl_2$ (2 mol%), CuI (4 mol%), and triethylamine (1.5 equiv.) under nitrogen atmosphere. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with saturated NH_4Cl and the organic layer was extracted with ethyl acetate (EtOAc). The combined organic extracts were thoroughly washed with brine (50 mL), dried over sodium sulfate, and then concentrated under reduced pressure. The resulting crude products were purified through flash column chromatography, to afford the desired products **S_{3a-l}** with excellent yield up to 90%.

General procedure C, for the synthesis of compounds from S_{3a-l} to 1a-l.



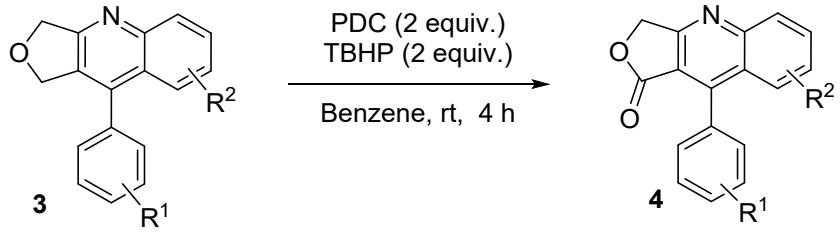
To a stirred solution of oxalyl chloride (1.2 equiv.) in dichloromethane (5 mL) at -78 °C, DMSO (2.4 equiv.) was added dropwise, and the reaction mixture was allowed to stir at the same temperature for 5 minutes. A solution of alcohol (1 equiv.) in 3 mL dichloromethane was then added to the reaction mixture. After 45 min of stirring, triethylamine (5 equiv.) was added, and after 5 minutes reaction mixture was warmed to ambient temperature for 2 h. The reaction mixture was then diluted with dichloromethane and water and the layers were separated. The organic layer was washed with water, brine, dried over $MgSO_4$, filtered and concentrated in vacuo. Without further purification, the respective aldehydes were used for further imino Diels- Alder reaction.

General procedure D, for the synthesis of compounds 3a-v from 1a-l.



To the crude solution of aldehyde (1 equiv.) and aniline (1 equiv.) in acetonitrile solvent was added $Cu(OTf)_2$ (0.05 mol%) and Oxone (1 equiv.) at room temperature. Then, the resulting reaction mixture was allowed to stir at same temperature for 12 h. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with saturated aqueous ammonium chloride solution and was extracted with water and ethyl acetate. The organic layer was then dried over Na_2SO_4 and evaporated under vacuo. The residue was separated by column chromatography using the mixture EtOAc/hexanes (1:2) to afford the desired dihydrofuroquinolines **3a-v.**

General procedure E, for the synthesis of compounds from 3c and 3f to 4a-b



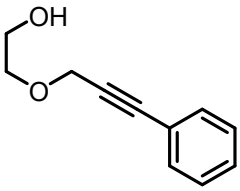
To a solution of dihydrofuroquinoline (0.439 mmol) in benzene was added Pyridinium dichromate (PDC, 0.087 mmol) at room temperature. The resulting suspension was stirred vigorously and a solution of *tertiary* butyl hydroperoxide in decane (5.0-6.0 M solution) was added dropwise over 15 min. The reaction mixture was then stirred further at room temperature for 4 h. After completion of the reaction (monitored by TLC), the reaction mixture was filtered. The resulting crude was purified by column chromatography on silica gel with hexane/ethyl acetate (9:1) to afford the desired oxidized products **4a-b**.

General procedure for the preparation of cross coupled Sonogashira products

The experimental and spectral data of compounds **S_{3a}, S_{3b}, S_{3c}, S_{3e},** and **S_{3i}** were reported in our previous work.[12e]

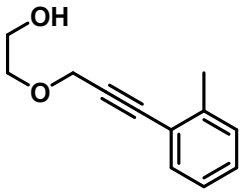
Synthesis of Sonagashira product (S_{3a}-S_{3l})

Synthesis of-2-((3-phenylprop-2-yn-1-yl) oxy) ethan-1-ol (S_{3a}).



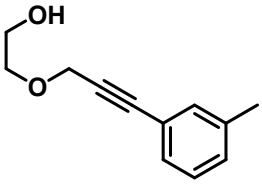
Following the general procedure **B**, **S_2** (1.00 gm, 10.00 mmol) in THF was allowed to react with iodobenzene (1.24 ml, 11.00 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (140 mg, 0.02 mmol), CuI (38 mg, 0.2 mmol), Et_3N (2.16 ml, 15.00 mmol) to afford compound **S_{3a}** in 85% yield (1.5 g); Yellowish oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.42 (m, 2H), 7.34 – 7.28 (m, 3H), 4.43 (s, 1H), 3.84 – 3.78 (m, J = 3.5 Hz, 2H), 3.72 (dd, 2H), 2.26 (bs, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.78, 128.57, 128.33, 122.46, 86.55, 84.79, 71.26, 61.79, 59.22.

Synthesis of-2-((3-(*o*-tolyl) prop-2-yn-1-yl) oxy) ethan-1-ol (S_{3b})



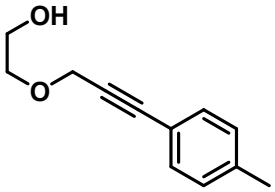
Following the general procedure **B**, **S_2** (1g, 10.0 mmol) in THF was allowed to react with 2-iodotoluene (1.41 ml, 11.00 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (140 mg, 0.02 mmol), CuI (38 mg, 0.02 mmol), Et_3N (2.16 ml, 15.00 mmol) to afford compound **S_{3b}** in 65% yield (1.25 g); Yellowish oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 7.4 Hz, 1H), 7.26 – 7.17 (m, 2H), 7.13 (ddd, J = 6.9, 4.6, 1.6 Hz, 1H), 4.48 (s, 2H), 3.80 (d, J = 7.0 Hz, 2H), 3.77 – 3.72 (m, 2H), 2.44 (s, 3H), 2.13 (bs, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.30, 132.15, 129.46, 128.56, 125.56, 122.26, 88.60, 85.47, 71.11, 61.84, 59.30, 20.73.

Synthesis of- 2-((3-(*m*-tolyl) prop-2-yn-1-yl) oxy) ethan-1-ol (S_{3c}).



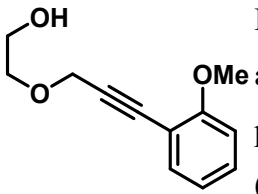
Following the general procedure **B**, **S_2** (1.0 g, 10.00 mmol) in THF was allowed to react with 4-iodotoluene (1.41 ml, 11.00 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (140 mg, 0.02 mmol), CuI (38 mg, 0.02 mmol), Et_3N (2.16 ml, 15.00 mmol) to afford compound **S_{3c}** in 72% yield (1.37 g); Yellowish oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (s, 1H), 7.25 (d, J = 8.0 Hz, 1H), 7.20 (t, J = 7.5 Hz, 1H), 7.14 (d, J = 7.5 Hz, 1H), 4.43 (s, 2H), 3.82 – 3.79 (m, 2H), 3.74 – 3.70 (m, 2H), 2.32 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.03, 132.35, 129.45, 128.83, 128.22, 122.25, 86.74, 84.40, 71.18, 61.84, 59.23, 21.19.

Synthesis of-2-((3-(*p*-tolyl) prop-2-yn-1-yl) oxy) ethan-1-ol (S_{3d}).



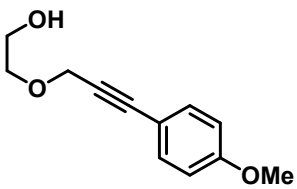
Following the general procedure **B**, **S_2** (1.0 g, 10.00 mmol) in THF was allowed to react with 4-iodotoluene (1.41 ml, 11.00 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (140 mg, 0.02 mmol), CuI (38 mg, 0.02 mmol), Et_3N (2.16 ml, 15.00 mmol) to afford compound **S_{3d}** in 72% yield (1.37 g); Yellowish oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, J = 8.1 Hz, 2H), 7.12 (d, J = 7.9 Hz, 2H), 4.42 (s, 2H), 3.83 – 3.78 (m, 2H), 3.74 – 3.70 (m, 2H), 2.34 (s, 3H), 2.22 (bs, J = 20.4, 6.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.72, 131.68, 129.09, 119.36, 86.69, 84.07, 71.20, 61.82, 59.27, 21.49.

Synthesis of-2-((3-(2-methoxyphenyl) prop-2-yn-1-yl) oxy) ethan-1-ol (S_{3e}).



Following the general procedure **B**, **S_2** (1.00g, 10.00 mmol) in THF was allowed to react with 2-iodo methoxybenzene (1.51 ml, 11.00 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (140 mg, 0.02 mmol), CuI (38 mg, 0.02 mmol), Et_3N (2.16 ml, 15.00 mmol) to afford compound **S_{3e}** in 62% yield (1.29 g); Yellowish oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (dd, J = 7.6, 1.7 Hz, 1H), 7.26 – 7.21 (m, 1H), 6.86 – 6.79 (m, 2H), 4.41 (s, 2H), 3.81 (s, 3H), 3.76 – 3.73 (m, 2H), 3.70 – 3.66 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.08, 133.72, 130.04, 120.46, 111.57, 110.58, 89.03, 82.87, 71.29, 61.88, 59.44, 55.77.

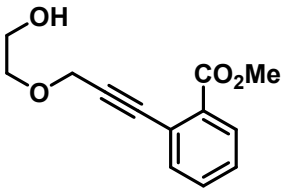
Synthesis of-2-((3-(4-methoxyphenyl)prop-2-yn-1-yl)oxy)ethan-1-ol (S_{3f}).



Following the general procedure **B**, **S_2** (1 g, 10.00 mmol) in THF was allowed to react with 2-iodo methoxybenzene (1.51 ml, 11.00 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (140 mg, 0.02 mmol), CuI (38 mg, 0.02 mmol), Et_3N (2.16 ml, 15.00 mmol) to afford compound **S_{3f}** in 62% yield (1.29 g);

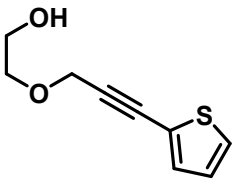
Yellowish oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (t, J = 5.7 Hz, 2H), 6.77 (t, J = 5.7 Hz, 2H), 4.35 (s, 2H), 3.74 (s, 3H), 3.72 (s, 2H), 3.67 – 3.62 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.81, 133.28, 114.53, 113.95, 86.49, 83.37, 71.14, 61.85, 59.31, 55.29, 29.70.

Synthesis of-methyl 2-(3-(2-hydroxyethoxy)prop-1-yn-1-yl)benzoate (S_{3g}).



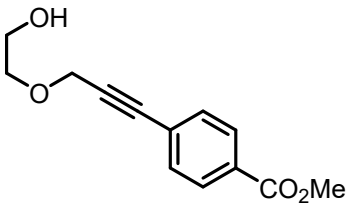
Following the general procedure **B**, S_2 (1 g, 10.00 mmol) in THF was allowed to react with Methyl-4-iodobenzoate (2.8 ml, 11.00 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (140 mg, 0.02 mmol), CuI (38 mg, 0.02 mmol), Et_3N (2.16 ml, 15.00 mmol) to afford compound S_{3g} in 61% yield (1.43 g); Yellowish oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.3 Hz, 2H), 7.47 (d, J = 8.3 Hz, 2H), 4.43 (s, 2H), 3.89 (s, 3H), 3.82 – 3.77 (m, 2H), 3.73 – 3.68 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.33, 153.44, 136.79, 135.03, 129.81, 128.56, 125.79, 120.85, 104.37, 72.55, 69.38, 61.89.

Synthesis of-2-((3-(thiophen-2-yl)prop-2-yn-1-yl)oxy)ethan-1-ol (S_{3h}).



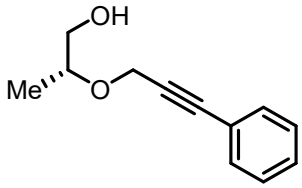
Following the general procedure **B**, S_2 (1 g, 10.00 mmol) in THF was allowed to react with 3-iodo nitrobenzene (2.7 g, 11.00 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (140 mg, 0.02 mmol), CuI (38 mg, 0.02 mmol), Et_3N (2.16 ml, 15.00 mmol) to afford compound S_{3h} in 73% yield (1.3 g); Yellowish oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 – 7.18 (m, 1H), 7.15 (dt, J = 5.1, 2.5 Hz, 1H), 6.90 (dd, J = 5.2, 3.6 Hz, 1H), 4.37 (s, 2H), 3.72 (d, J = 4.3 Hz, 2H), 3.66 – 3.61 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 132.56, 127.51, 126.98, 122.34, 88.81, 79.83, 71.28, 61.90, 59.28.

Synthesis of methyl 2-(3-(2-hydroxyethoxy) prop-1-yn-1-yl) benzoate (S_{3i}).



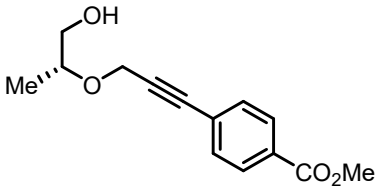
Following the general procedure **B, S_2** (1 g, 10.00 mmol) in THF was allowed to react with Methyl-4-iodobenzoate (2.8 ml, 11.00 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (140 mg, 0.02 mmol), CuI (38 mg, 0.02 mmol), Et_3N (2.16 ml, 15.00 mmol) to afford compound S_{3i} in 61% yield (1.43 g); Yellowish oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.3 Hz, 2H), 7.47 (d, J = 8.3 Hz, 2H), 4.43 (s, 2H), 3.89 (s, 3H), 3.82 – 3.77 (m, 2H), 3.73 – 3.68 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.46, 131.64, 129.82, 129.46, 127.14, 87.87, 85.72, 71.41, 61.72, 59.11, 52.24.

Synthesis of (*R*)-2-((3-phenylprop-2-yn-1-yl)oxy)propan-1-ol (S_{3j}).



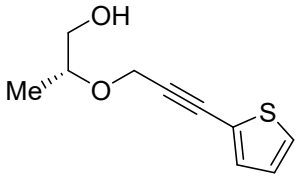
Following the general procedure **B, S_2** (0.5 g, 4.38 mmol) in THF was allowed to react with iodobenzoate (0.98 g, 4.81 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (56 mg, 0.02 mmol), CuI (16 mg, 0.02 mmol), Et_3N (0.9 ml, 6.57 mmol) to afford compound **S_{3j}** in 61% yield (0.40 g); Yellowish oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 – 7.39 (m, 2H), 7.33 – 7.28 (m, 3H), 4.49 (d, J = 15.8 Hz, 1H), 4.39 (d, J = 15.9 Hz, 1H), 3.89 – 3.80 (m, 1H), 3.64 (d, J = 3.3 Hz, 1H), 3.52 (dd, J = 11.6, 7.0 Hz, 1H), 1.19 (d, J = 6.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 131.86, 131.83, 128.64, 128.60, 128.40, 122.59, 86.60, 86.18, 85.43, 84.87, 75.69, 75.60, 66.55, 66.40, 59.36, 57.07, 29.78, 18.75, 17.78, 15.80.

Synthesis of methyl (*R*)-4-(3-((1-hydroxypropan-2-yl)oxy)prop-1-yn-1-yl)benzoate (S_{3k}).



Following the general procedure **B, S_2** (0.5 g, 4.38 mmol) in THF was allowed to react with Methyl-4-iodobenzoate (1.2 g, 4.81 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (56 mg, 0.02 mmol), CuI (16 mg, 0.02 mmol), Et_3N (0.9 ml, 6.57 mmol) to afford compound **S_{3k}** in 68% yield (0.73 g); Yellowish oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, 2H), 7.47 (d, 2H), 4.49 (d, J = 16.0 Hz, 1H), 4.43 – 4.37 (m, 1H), 3.89 (s, 3H), 3.86 – 3.78 (m, 1H), 3.64 (dd, J = 11.6, 3.3 Hz, 1H), 3.53 (d, J = 7.0 Hz, 1H), 1.18 (d, J = 6.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.55, 131.72, 129.89, 129.55, 127.27, 88.52, 85.38, 75.79, 66.37, 59.27, 56.98, 52.32, 18.79, 15.77.

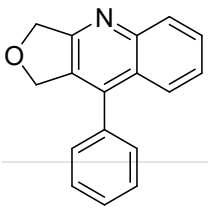
Synthesis of (*R*)-2-((3-(thiophen-2-yl)prop-2-yn-1-yl)oxy)propan-1-ol (S_{3l}).



Following the general procedure **B, S_2** (0.5 g, 4.38 mmol) in THF was allowed to react with 2-iodothophene (1.0 g, 4.81 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (56 mg, 0.02 mmol), CuI (16 mg, 0.02 mmol), Et_3N (0.9 ml, 6.57 mmol) to afford compound **S_{3l}** in 45% yield (0.37 g); Yellowish oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, J = 1.7 Hz, 1H), 7.21 (d, J = 1.2 Hz, 1H), 6.95 (dd, J = 5.1, 3.6 Hz, 1H), 4.49 (d, J = 16.1 Hz, 1H), 4.39 (d, J = 16.0 Hz, 1H), 3.86 – 3.76 (m, 1H), 3.63 (dd, J = 11.7, 3.3 Hz, 1H), 3.51 (dd, J = 11.6, 7.0 Hz, 1H), 1.17 (d, J = 6.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 132.58, 127.51, 127.03, 122.50, 89.43, 79.44, 75.64, 66.37, 57.11, 15.77.

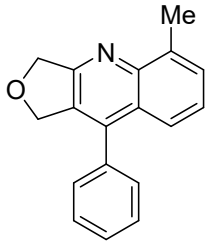
Synthesis of dihydrofuroquinoline (3a-v)

Synthesis of 9-phenyl-1,3-dihydrofuro[3,4-*b*]quinoline (3a).



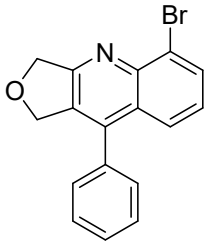
Following the general procedure **D**, **1a** (150 mg, 0.86 mmol) in acetonitrile was allowed to react with aniline **(2a),** (0.078 ml, 0.86 mmol) in the presence of $Cu(OTf)_2$ (15.56 mg, 0.043 mmol), Oxone (264.63 mg, 0.86 mmol), to afford compound **3a** in 72% yield (207 mg); White solid; mp 209 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 8.10 (d, J = 8.2 Hz, 1H), 7.76 – 7.73 (m, 1H), 7.69 (ddd, J = 8.3, 6.9, 1.3 Hz, 1H), 7.55 – 7.50 (m, 2H), 7.49 (dt, J = 5.7, 2.3 Hz, 1H), 7.47 – 7.43 (m, 1H), 7.38 – 7.36 (m, 2H), 5.23 (s, 2H), 5.12 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.30, 148.82, 141.43, 135.64, 129.31, 129.19, 128.96, 129.03, 128.93, 128.76, 126.46, 126.15, 125.82, 73.16, 71.90; HRMS (ESI): *m/z* calcd for $C_{17}H_{14}NO$ $[M+H]^+$; 248.1075, found: 248.1075.

Synthesis of 5-methyl-9-phenyl-1,3-dihydrofuro[3,4-*b*]quinoline (3b).



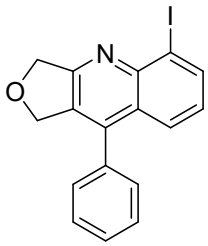
Following the general procedure **D**, **1i** (200 mg, 1.06 mmol) in acetonitrile was allowed to react with *ortho*-toluidine (64 mg, 1.06 mmol) in the presence of $Cu(OTf)_2$ (19 mg, 0.05 mmol), Oxone (325 mg, 1.06 mmol), to afford compound **3b** in 47% yield (132 mg); Yellow Solid; mp 133 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, 1H), 7.56 – 7.45 (m, 4H), 7.38 – 7.30 (m, 3H), 5.27 (s, 2H), 5.12 (s, 2H), 2.84 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.12, 136.96, 136.15, 129.60, 128.96, 128.87, 128.67, 128.61, 126.11, 125.97, 123.84, 73.41, 71.90, 18.72; HRMS (ESI): *m/z* calcd for $C_{18}H_{16}NO$ $[M+H]^+$; 262.1231, found: 262.1233.

Synthesis of 5-bromo-9-phenyl-1,3-dihydrofuro[3,4-*b*]quinoline (3c).



Following the general procedure **D**, **1a** (150 mg, 0.86 mmol) in acetonitrile was allowed to react with 2-Bromo aniline **(2b),** (148 mg, 0.86 mmol) in the presence of $Cu(OTf)_2$ (15.56 mg, 0.043 mmol), Oxone (264.63 mg, 0.86 mmol), to afford compound **3c** in 75% yield (210 mg); White solid; mp 271 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (dd, J = 7.4, 1.0 Hz, 1H), 7.72 (dd, J = 8.4, 1.1 Hz, 1H), 7.58 – 7.48 (m, 3H), 7.36 (dd, J = 7.8, 1.6 Hz, 2H), 7.30 (t, 1H), 5.32 (s, 2H), 5.13 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.53, 145.97, 141.86, 135.24, 133.02, 130.04, 128.96, 128.90, 128.82, 127.76, 126.54, 125.77, 124.68, 73.31, 71.66; HRMS (ESI): *m/z* calcd. for $C_{17}H_{13}NOBr$ $[M+H]^+$; 326.0180, found: 326.0183.

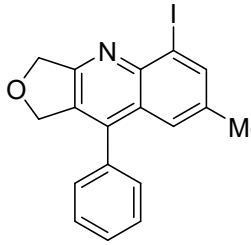
Synthesis of 5-iodo-9-phenyl-1,3-dihydrofuro[3,4-*b*] quinoline (3d).



Following the general procedure **D**, **1a** (150 mg, 0.86 mmol) in acetonitrile was allowed to react with 2-iodo aniline **(2c),** (188.77 mg, 0.86 mmol) in the presence of $Cu(OTf)_2$ (15.56 mg, 0.043 mmol), Oxone (264.63 mg, 0.86 mmol), to afford

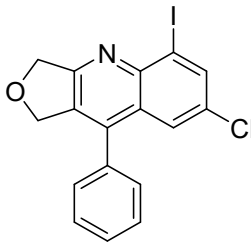
compound **3d** in 80% yield (260 mg); White solid; mp 143 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 7.2 Hz, 1H), 7.73 (d, J = 8.3 Hz, 1H), 7.58 – 7.47 (m, 3H), 7.35 (d, J = 6.6 Hz, 2H), 7.16 (t, J = 7.8 Hz, 1H), 5.31 (s, 2H), 5.12 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.65, 147.69, 141.87, 139.93, 135.15, 130.02, 128.95, 128.85, 127.35, 127.01, 126.72, 103.18, 73.18, 71.67; HRMS (ESI): *m/z* calcd for $C_{17}H_{13}NOI$ $[M+H]^+$; 374.0041, found: 374.0041.

Synthesis of 5-iodo-7-methyl-9-phenyl-1,3-dihydrofuro[3,4-*b*] quinoline (3e).



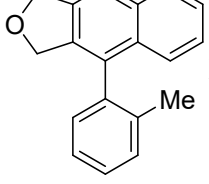
Following the general procedure **D**, **3a** (150 mg, 0.86 mmol) in acetonitrile was allowed to react with 2-Iodo-4-methylaniline **(2d),** (200.84 mg, 0.86 mmol) in the presence of $Cu(OTf)_2$ (15.56 mg, 0.043 mmol), Oxone (264.63 mg, 0.086 mmol), to afford compound **3e** in 78% yield (262 mg); White solid; mp 133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 1.5 Hz, 1H), 7.58 – 7.50 (m, 3H), 7.46 (s, 1H), 7.34 (dd, J = 7.8, 1.5 Hz, 2H), 5.30 (s, 2H), 5.10 (s, 2H), 2.39 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.94, 141.57, 137.19, 136.48, 132.78, 130.66, 125.29, 124.23, 124.13, 124.03, 122.01, 120.98, 98.14, 68.44, 66.99, 16.40; HRMS (ESI): *m/z* calcd for $C_{18}H_{15}INO$ $[M+H]^+$; 388.0198, found: 388.0199.

Synthesis of 5-iodo-9-phenyl-7-(trifluoromethyl)-1,3-dihydrofuro[3,4-*b*]quinoline (3f).



Following the general procedure **D**, **1a** (150 mg, 0.86 mmol) in acetonitrile was allowed to react with 2-Iodo-4-(trifluoromethyl)aniline **(2e),** (247.4 mg, 0.086 mmol) in the presence of $Cu(OTf)_2$ (15.56 mg, 0.043 mmol), Oxone (264.63 mg, 0.86 mmol), to afford compound **3f** in 55% yield (210 mg); White solid; mp 168 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H), 8.04 (s, 1H), 7.64 – 7.51 (m, 3H), 7.36 (d, J = 7.3 Hz, 2H), 5.33 (s, 2H), 5.15 (s, 2H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.07. ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.06, 148.94, 142.79, 135.46 (q, 3.2 Hz) 132.77 (q, 273.0 Hz), 129.41, 129.08 (q, 35.6 Hz) 128.75, 125.75, 124.44 (q, 4.2 Hz) 124.32, 121.61, 104.14, 73.16, 71.58; HRMS (ESI): *m/z* calcd for $C_{18}H_{12}F_3INO$ $[M+H]^+$; 441.9915, found: 441.9917.

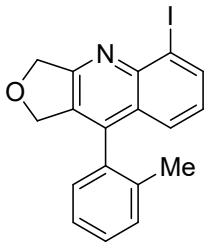
Synthesis of 5-bromo-9-(*o*-tolyl)-1,3-dihydrofuro[3,4-*b*] quinoline (3g).



Following the general procedure **D**, **1b** (125 mg, 0.66 mmol) in acetonitrile was allowed to react with 2-Bromo aniline **(2b),** (115.53 mg, 0.66 mmol) in the presence of $Cu(OTf)_2$ (12.0 mg, 0.033 mmol), Oxone (203.8 mg, 0.66 mmol), to afford compound **3g** in 55% yield (125 mg); White solid; mp 165 °C; ^{1}H NMR

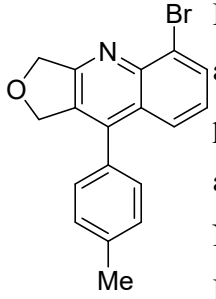
(400 MHz, $CDCl_3$) δ 8.04 (dd, J = 7.4, 1.3 Hz, 1H), 7.43 – 7.36 (m, 3H), 7.33 (dd, J = 11.5, 4.3 Hz, 1H), 7.29 (d, J = 7.5 Hz, 1H), 7.14 (d, J = 6.8 Hz, 1H), 5.36 (s, 2H), 5.07 (d, J = 13.9 Hz, 1H), 4.93 (d, J = 13.9 Hz, 1H), 1.98 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.72, 145.83, 141.88, 135.68, 134.71, 133.17, 130.70, 130.42, 129.10, 128.52, 128.09, 126.79, 126.44, 125.65, 124.80, 73.40, 71.67, 19.68; HRMS (ESI): m/z calcd for $C_{18}H_{15}NOBr$ $[M+H]^+$; 340.0337, found: 340.0332.

Synthesis of 5-iodo-9-(*o*-tolyl)-1,3-dihydrofuro[3,4-*b*] quinoline (3h).



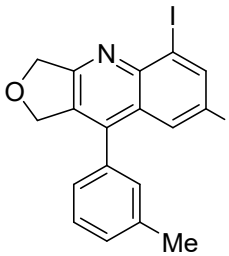
Following the general procedure **D**, **1b** (150 mg, 0.79 mmol) in acetonitrile was allowed to react with 2-Iodo aniline **(2c),** (174.54 mg, 0.79 mmol) in the presence of $Cu(OTf)_2$ (14.4 mg, 0.039 mmol), Oxone (244.68 mg, 0.79 mmol), to afford compound **3h** in 60% yield (155 mg); White solid; mp 151 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (dd, J = 7.3, 1.1 Hz, 1H), 7.45 – 7.39 (m, 2H), 7.39 – 7.31 (m, 2H), 7.17 – 7.11 (m, 2H), 5.35 (s, 2H), 5.06 (d, J = 13.9 Hz, 1H), 4.93 (d, J = 13.9 Hz, 1H), 1.97 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.75, 147.37, 141.98, 140.09, 135.63, 134.49, 130.61, 130.37, 129.01, 128.46, 127.56, 127.30, 126.55, 126.36, 102.99, 73.21, 71.60, 19.64; HRMS (ESI): *m/z* calcd. for $C_{18}H_{15}NOI$ $[M+H]^+$; 388.0198, found: 388.0193.

Synthesis of 5-bromo-9-(*p*-tolyl)-1,3-dihydrofuro[3,4-*b*]quinoline (3i).



Following the general procedure **D**, **3c** (250 mg, 1.33 mmol) in acetonitrile was allowed to react with 2-Bromo aniline **(2b),** (228.58 mg, 1.33 mmol) in the presence of $Cu(OTf)_2$ (23.8 mg, 0.066 mmol), Oxone (408 mg, 1.33 mmol), to afford compound **3i** in 62% yield (280 mg); Pale-yellow solid; mp 192 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (dd, J = 7.4, 1.2 Hz, 1H), 7.76 (dd, J = 8.4, 1.2 Hz, 1H), 7.35 (d, J = 7.9 Hz, 2H), 7.30 (t, J = 9.9, 6.0 Hz, 1H), 7.26 (d, J = 7.5 Hz, 3H), 5.33 (s, 2H), 5.14 (s, 2H), 2.47 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.46, 142.22, 138.94, 133.06, 132.15, 130.10, 129.65, 128.76, 127.92, 126.50, 125.88, 73.33, 71.74, 21.40; HRMS (ESI): m/z calcd. for $C_{18}H_{15}NOBr$ $[M+H]^+$; 340.0337, found: 340.0332.

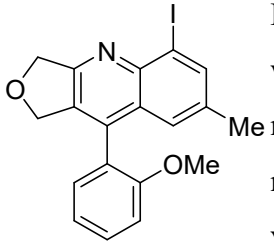
Synthesis of 5-iodo-7-methyl-9-(*m*-tolyl)-1,3-dihydrofuro[3,4-*b*]quinoline (3j).



Following the general procedure **D**, **1d** (200 mg, 1.15 mmol) in acetonitrile was allowed to react with 2-iodo-4-methylaniline **(2d),** (267.8 gm, 1.15 mmol) in the presence of $Cu(OTf)_2$ (20.74 mg, 0.57 mmol), Oxone (352.8 mg, 1.15 mmol), to afford compound **3j** in 65% yield (277 mg); Yellowish

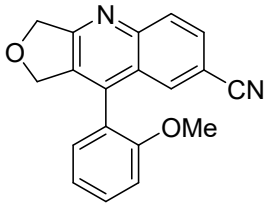
oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 1.7 Hz, 1H), 7.39 (dd, J = 5.5, 0.8 Hz, 1H), 7.34 (d, J = 8.1 Hz, 1H), 7.24 (d, J = 7.5 Hz, 1H), 7.06 (d, J = 7.3 Hz, 2H), 5.23 (s, 2H), 5.02 (s, 2H), 2.37 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.57, 146.03, 142.01, 141.69, 138.73, 137.51, 135.24, 130.05, 129.53, 129.29, 128.82, 126.87, 125.89, 125.81, 102.44, 73.15, 71.73, 21.57, 21.14; HRMS (ESI): *m/z* calcd for $C_{19}H_{17}NOI$ $[M+H]^+$; 402.0354, found: 402.0349.

Synthesis of 5-iodo-9-(2-methoxyphenyl)-7-methyl-1,3-dihydrofuro[3,4-*b*]quinoline (3k).



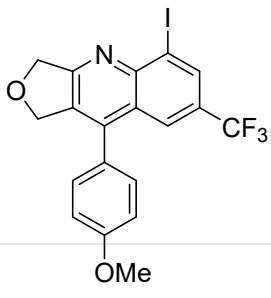
Following the general procedure **D**, **1e** (150 mg, 0.73 mmol) in acetonitrile was allowed to react with 2-iodo-4-methylaniline **(2d),** (171.3 mg, 0.73 mmol) in the presence of $Cu(OTf)_2$ (13.27 mg, 0.036 mmol), Oxone (225.7 mg, 0.73 mmol), to afford compound **3k** in 60% yield (185 mg); Brownish yellow solid; mp 191 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (t, J = 7.8 Hz, 1H), 7.32 (s, 1H), 7.17 (d, J = 7.3 Hz, 1H), 7.09 (dd, J = 13.4, 7.8 Hz, 2H), 5.29 (s, 2H), 5.01 (d, J = 10.6 Hz, 2H), 3.73 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.44, 156.53, 146.14, 141.66, 138.10, 137.16, 130.98, 130.67, 130.39, 127.22, 125.78, 123.65, 120.81, 111.40, 102.74, 73.15, 71.95, 55.50, 21.07; HRMS (ESI): *m/z* calcd for $C_{19}H_{17}INO_2$ $[M+H]^+$; 418.0304, found: 418.0585.

Synthesis of 9-(2-methoxyphenyl)-1,3-dihydrofuro[3,4-b]quinoline-7-carbonitrile (3l).



Following the general procedure **D**, **1e** (150 mg, 0.73 mmol) in acetonitrile was allowed to react with 4-aminobenzonitrile **(2f),** (86.7 mg, 0.73 mmol) in the presence of $Cu(OTf)_2$ (13.24 mg, 0.036 mmol), Oxone (225.7 mg, 0.73 mmol), to afford compound **3l** in 68% yield (151mg); White solid; mp 174 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 8.7 Hz, 1H), 7.99 (d, J = 1.4 Hz, 1H), 7.82 (dd, J = 8.7, 1.6 Hz, 1H), 7.58 – 7.51 (m, 1H), 7.18 (dd, J = 7.4, 2.0 Hz, 1H), 7.14 (dd, J = 13.0, 7.8 Hz, 2H), 5.26 (s, 2H), 5.07 (s, 2H), 3.76 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.62, 156.40, 149.73, 138.90, 133.82, 132.54, 131.97, 131.18, 130.56, 130.48, 129.70, 126.39, 121.12, 114.43, 111.58, 109.70, 73.08, 71.91, 55.50; HRMS (ESI): *m/z* calcd for $C_{19}H_{15}N_2O_2$ $[M+H]^+$; 303.1133, found: 303.1128.

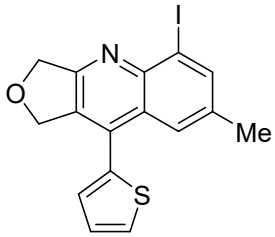
Synthesis of 5-iodo-9-(4-methoxyphenyl)-7-(trifluoromethyl)-1,3-dihydrofuro[3,4-*b*] quinoline (3m).



Following the general procedure **D**, **1f** (150 mg, 0.73 mmol) in acetonitrile was allowed to react with 2-iodo-4-(trifluoromethyl)aniline **(2e),** (210.9 gm,

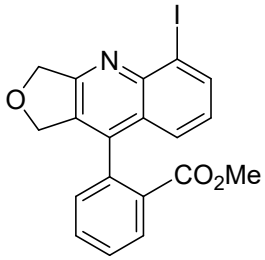
0.73 mmol) in the presence of $Cu(OTf)_2$ (13.24 mg, 0.036 mmol), Oxone (225.7 mg, 0.73 mmol), to afford compound **3m** in 45% yield (157 mg); White solid; mp 97 °C; ^{1}H NMR (500 MHz,) δ 8.46 (d, J = 2.4 Hz, 2H), 8.11 – 8.05 (m, 2H), 7.32 – 7.22 (m 1H), 7.11 – 7.03 (m, 1H), 5.31 (s,2H), 5.16 (s, 2H), 3.91 (s, 3H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.02. ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.04, 160.41, 142.80, 135.47, 135.44 (q, 3.5 Hz) 131.44 (q, 270 Hz)130.30, 128.84 (q, 32 Hz) 126.14, 126.05, 124.68, (4.2 Hz) 124.64, 114.78, 104.15, 73.29, 71.81, 55.53.; HRMS (ESI): *m/z* calcd for $C_{19}H_{14}F_3INO_2$ $[M+H]^+$; 472.0021, found: 472.0244.

Synthesis of 5-iodo-7-methyl-9-(thiophen-2-yl)-1,3-dihydrofuro[3,4-*b*]quinoline (3n).



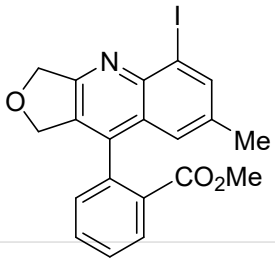
Following the general procedure **D**, **1g** (150 mg, 0.83 mmol) in acetonitrile was allowed to react with 2-iodo-4-methylaniline **(2d),** (194 mg, 0.83 mmol) in the presence of $Cu(OTf)_2$ (15.04 mg, 0.04 mmol), Oxone (255.83 mg, 0.83 mmol), to afford compound **3n** in 58% yield (190 mg); Pale yellow solid; mp 190 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.82 (s, 1H), 7.57 (d, J = 5.0 Hz, 1H), 7.28 – 7.23 (m, 1H), 7.21 (d, J = 3.3 Hz, 1H), 5.28 (s, 2H), 5.24 (s, 2H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.53, 146.34, 142.06, 137.81, 135.12, 134.16, 130.84, 129.18, 127.74, 127.63, 126.84, 125.56, 102.88, 73.21, 72.22; HRMS (ESI): *m/z* calcd for $C_{16}H_{13}INOS$ $[M+H]^+$; 393.9762, found: 393.9995.

Synthesis of methyl 2-(5-iodo-1,3-dihydrofuro[3,4-*b*] quinolin-9-yl) benzoate (3o).



Following the general procedure **D**, **1h** (300 mg, 1.29 mmol) in acetonitrile was allowed to react with 2-iodoaniline **(2c),** (283.19 mg, 1.29 mmol) in the presence of $Cu(OTf)_2$ (15.04 mg, 0.04 mmol), Oxone (397.0 mg, 1.29 mmol), to afford compound **3o** in 62% yield (326 mg); Greyish black oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 – 8.26 (m, 1H), 8.18 – 8.14 (m, 1H), 7.69 – 7.64 (m, 1H), 7.62 – 7.57 (m, 1H), 7.34 – 7.31 (m 1H), 7.24 – 7.22 (m, 1H), 7.11 – 7.06 (m, 1H), 5.31 (s, 2H), 4.96 (q, J = 13.6 Hz, 2H), 3.50 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.35, 163.44, 147.29, 142.10, 139.82, 136.36, 132.79, 131.17, 130.29, 129.88, 129.66, 129.13, 127.38, 126.18, 103.35, 73.26, 71.58, 52.25, 29.77; HRMS (ESI): *m/z* calcd for $C_{19}H_{15}INO_3$ $[M+H]^+$; 432.0096, found: 432.0099.

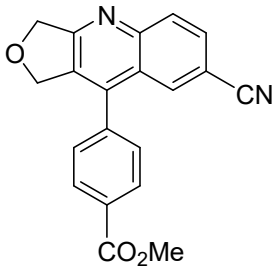
Synthesis of methyl 2-(5-iodo-7-methyl-1,3-dihydrofuro[3,4-*b*]quinolin-9-yl) benzoate 3p.



Following the general procedure **D**, **1h** (300 mg, 1.29 mmol) in acetonitrile was allowed to react with 2-iodo-4-methylaniline **(2d),** (300.57 mg, 1.29

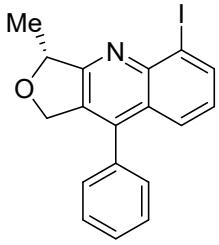
mmol) in the presence of $Cu(OTf)_2$ (15.04 mg, 0.04 mmol), Oxone (397.0 mg, 1.29 mmol), to afford compound **3p** in 65% yield (380 mg); Yellowish liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 – 8.13 (m, 2H), 7.70 – 7.64 (m, 1H), 7.62 – 7.57 (m, 1H), 7.24 – 7.20 (m, 1H), 7.05 (s, 1H), 5.30 – 5.27 (m, 2H), 4.91 (t, J = 6.6 Hz, 2H), 3.51 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.42, 162.39, 158.82, 145.91, 141.82, 141.38, 139.23, 137.49, 136.54, 132.77, 131.17, 130.35, 130.07, 129.83, 129.59, 129.03, 126.97, 125.22, 122.11, 103.03, 73.21, 71.60, 52.24, 29.77, 21.12; HRMS (ESI): *m/z* calcd for $C_{20}H_{17}INO_3$ $[M+H]^+$; 446.0253, found: 446.0484.

Synthesis of methyl 4-(7-cyano-1,3-dihydrofuro[3,4-*b*]quinolin-9-yl)benzoate (3q).



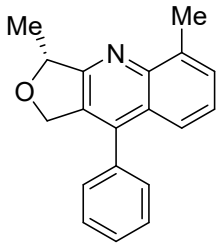
Following the general procedure **D**, **1i** (300 mg, 1.29 mmol) in acetonitrile was allowed to react with 4-aminobenzonitrile **(2f),** (152.22 mg, 1.29 mmol) in the presence of $Cu(OTf)_2$ (15.04 mg, 0.04 mmol), Oxone (397.0 mg, 1.29 mmol), to afford compound **3q** in 61% yield (220 mg); Yellowish oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 – 8.24 (m, 2H), 8.20 (d, J = 8.7 Hz, 1H), 8.04 (d, J = 1.6 Hz, 1H), 7.86 (dd, J = 8.7, 1.8 Hz, 1H), 7.46 – 7.43 (m, 2H), 5.25 (s, 2H), 5.13 (s, 2H), 3.99 (s, J = 2.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.30, 165.88, 138.65, 131.79, 131.73, 131.36, 130.89, 130.61, 130.34, 129.55, 128.94, 118.56, 110.58, 73.08, 71.48, 52.59, 29.77; HRMS (ESI): *m/z* calcd for $C_{20}H_{15}N_2O_3$ $[M+H]^+$; 331.1082, found: 331.1082.

Synthesis of (*R*)-5-iodo-3-methyl-9-phenyl-1,3-dihydrofuro[3,4-*b*]quinoline 3r.



Following the general procedure **D**, **1i** (250 mg, 1.32 mmol) in acetonitrile was allowed to react with 2-Iodo aniline **(2c)** (288 mg, 1.32 mmol) in the presence of $Cu(OTf)_2$ (22 mg, 0.06 mmol), Oxone (405.0 mg, 1.32 mmol), to afford compound **3r** in 41% yield (135 mg); Yellowish oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, J = 1.3 Hz, 1H), 7.73 (d, J = 1.3 Hz, 1H), 7.55 – 7.47 (m, 3H), 7.37 – 7.33 (m, 2H), 7.15 (dd, J = 8.4, 7.3 Hz, 1H), 5.46 – 5.40 (m, 1H), 5.06 (s, 2H), 1.73 (d, J = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.22, 147.55, 142.10, 139.96, 135.27, 130.18, 129.01, 128.97, 128.91, 127.44, 127.18, 126.72, 103.48, 79.28, 69.84, 20.22; HRMS (ESI): *m/z* calcd for $C_{18}H_{15}INO$ $[M+H]^+$; 388.0198, found: 388.0199.

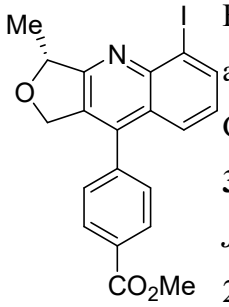
Synthesis of (*R*)-3,5-dimethyl-9-phenyl-1,3-dihydrofuro[3,4-*b*]quinoline (3s).



Following the general procedure **D**, **1i** (250 mg, 1.32 mmol) in acetonitrile was allowed to react with Ortho-toluidine **(2g)** (141 mg, 1.32 mmol) in the presence of $Cu(OTf)_2$ (22 mg, 0.06 mmol), Oxone (405 mg, 1.32 mmol), to afford

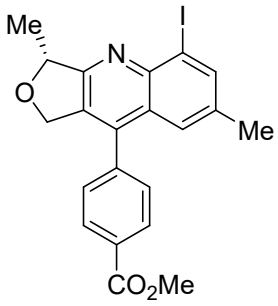
compound **3s** in 52% yield (190 mg); Yellow Viscous liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, 1H), 7.55 – 7.44 (m, 4H), 7.38 – 7.35 (m, 2H), 7.35 – 7.30 (m, 1H), 5.39 (q, J = 6.5 Hz, 1H), 5.06 (s, 2H), 2.86 (s, 3H), 1.70 (d, J = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.73, 137.24, 136.26, 129.37, 129.02, 128.83, 128.61, 128.53, 126.16, 125.88, 123.71, 79.39, 69.95, 20.35, 18.49; HRMS (ESI): *m/z* calcd for $C_{19}H_{18}NO$ $[M+H]^+$; 276.1388, found: 276.1390.

Synthesis of methyl (*R*)-4-(5-iodo-3-methyl-1,3-dihydrofuro[3,4-*b*]quinolin-9-yl)benzoate (3t).



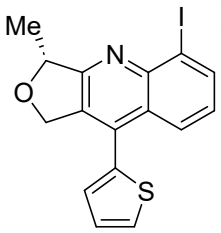
Following the general procedure **D**, **1i** (150 mg, 0.6 mmol) in acetonitrile was allowed to react with 2-Iodo aniline **(2c)** (130 mg, 0.6 mmol) in the presence of $Cu(OTf)_2$ (11.0 mg, 0.03 mmol), Oxone (184 mg, 0.6 mmol), to afford compound **3t** in 55% yield (200 mg); Yellowish oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, J = 1.2 Hz, 1H), 8.24 – 8.17 (m, 2H), 7.64 (d, J = 1.3 Hz, 1H), 7.46 – 7.42 (m, 2H), 7.16 (dd, J = 8.4, 7.3 Hz, 1H), 5.45 – 5.37 (m, 1H), 5.03 (d, J = 1.0 Hz, 2H), 3.97 (s, 3H), 1.72 (d, J = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.57, 166.27, 147.66, 140.74, 140.06, 139.99, 130.71, 130.26, 130.09, 129.13, 127.69, 126.63, 126.26, 103.89, 79.26, 69.65, 52.50, 20.15; HRMS (ESI): *m/z* calcd for $C_{20}H_{17}INO_3$ $[M+H]^+$; 446.0253, found: 446.0255.

Synthesis of methyl (*R*)-4-(5-iodo-3,7-dimethyl-1,3-dihydrofuro[3,4-*b*]quinolin-9-yl)benzoate 3u.



Following the general procedure **D**, **1i** (150 mg, 0.6 mmol) in acetonitrile was allowed to react with 4-Amono-3-iodotoluene **(2d)** (140 mg, 0.6 mmol) in the presence of $Cu(OTf)_2$ (11.0 mg, 0.03 mmol), Oxone (184 mg, 0.6 mmol), to afford compound **3u** in 64% yield (178 mg); Yellowish oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 – 8.19 (m, 2H), 8.18 (d, J = 1.8 Hz, 1H), 7.45 – 7.41 (m, 2H), 7.36 (dq, J = 1.9, 1.0 Hz, 1H), 5.40 (q, J = 6.5 Hz, 1H), 5.00 (d, J = 1.0 Hz, 2H), 3.97 (s, 3H), 2.38 (s, 3H), 1.71 (d, J = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.63, 165.28, 146.20, 142.01, 140.20, 140.05, 137.88, 130.63, 130.25, 130.01, 129.12, 126.34, 125.26, 103.50, 79.20, 69.67, 52.48, 21.20, 20.18; HRMS (ESI): *m/z* calcd for $C_{21}H_{19}INO_3$ $[M+H]^+$; 460.0409, found: 460.0410.

Synthesis of (*R*)-5-iodo-3-methyl-9-(thiophen-2-yl)-1,3-dihydrofuro[3,4-*b*]quinoline (3v).

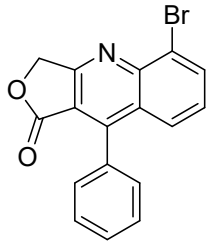


Following the general procedure **D**, **1i** (150 mg, 0.85 mmol) in acetonitrile was allowed to react with 2-Iodo aniline **(2c)** (185 mg, 0.85 mmol) in the presence of

$Cu(OTf)_2$ (15.0 mg, 0.04 mmol), Oxone (262 mg, 0.85 mmol), to afford compound **3v** in 39% yield (130 mg); Yellowish oil; mp 207 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, J = 1.3 Hz, 1H), 8.08 (dd, J = 8.4, 1.3 Hz, 1H), 7.56 (d, J = 1.3 Hz, 1H), 7.24 – 7.18 (m, 3H), 5.46 – 5.38 (m, 1H), 5.25 – 5.15 (m, 2H), 1.72 (d, J = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.15, 147.80, 140.03, 135.12, 134.86, 130.92, 129.42, 127.83, 127.67, 127.22, 126.54, 103.82, 79.36, 70.41, 20.19, -17.30; HRMS (ESI): *m/z* calcd for $C_{16}H_{13}INOS$ $[M+H]^+$; 393.9762, found: 393.9763.

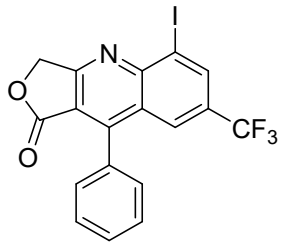
Synthesis of Lactone (4a-b)

Synthesis of 5-bromo-9-phenylfuro[3,4-*b*]quinolin-1(3H)-one 4a.



Following the general procedure **E**, **3c** (200 mg, 0.61 mmol) in benzene was allowed to react with Pyridinium Dichromate (40 mg, 0.12 mmol) and tert-butyl hydroperoxide (0.01 ml, 0.12 mmol), to afford compound **4a** in 67% yield (140 mg); Pale yellowish solid; mp 227 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (dd, J = 7.4, 1.3 Hz, 1H), 7.88 (dd, J = 8.5, 1.3 Hz, 1H), 7.62 – 7.53 (m, 3H), 7.47 – 7.38 (m, 3H), 5.53 (s, 2H). ^{13}C NMR (126 MHz) δ 167.69, 164.67, 152.53, 148.35, 140.01, 136.30, 129.92, 129.19, 128.84, 128.29, 128.24, 127.56, 124.80, 114.28, 69.87; HRMS (ESI): *m/z* calcd for $C_{17}H_{11}NO_2$ $[M+H]^+$; 338.9894, found: 339.9968.

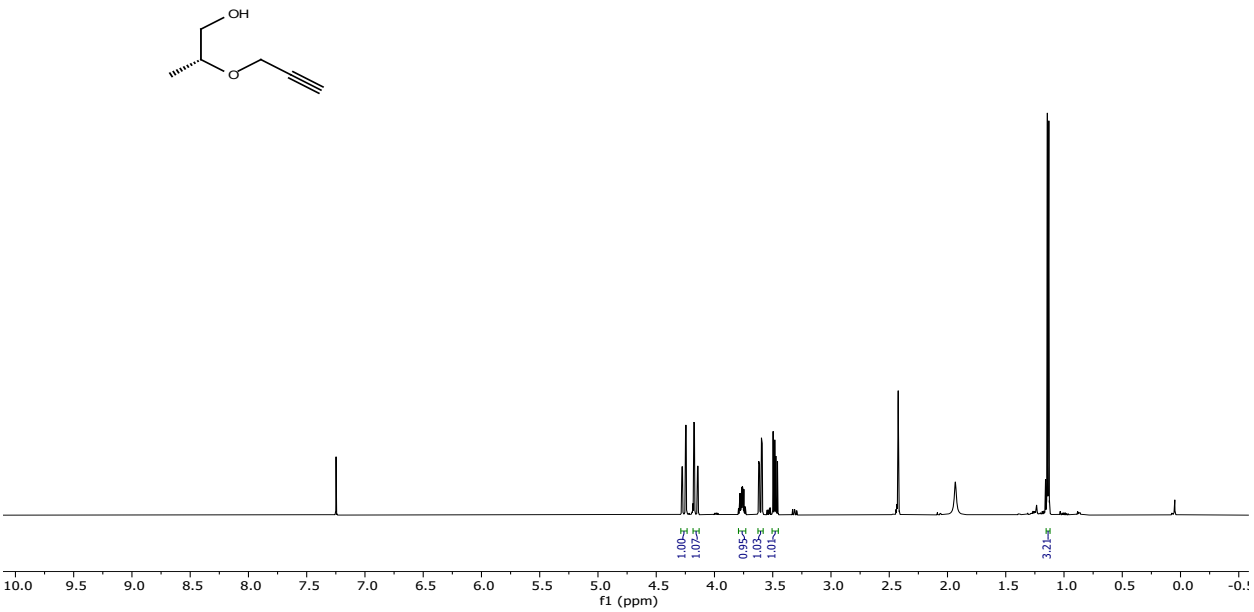
Synthesis - of 5-iodo-9-phenyl-7-(trifluoromethyl)furo[3,4-*b*]quinolin-1(3H)-one (4b).



Following the general procedure **E**, **3f** (260 mg, 0.58 mmol) in benzene was allowed to react with Pyridinium Dichromate (44.33 mg, 0.11 mmol) and tert-butyl hydroperoxide (0.01 ml, 0.11 mmol), to afford compound **4b** in 78% yield (210 mg); White solid; mp 187 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 (d, J = 1.9 Hz, 1H), 8.19 (dd, J = 1.8, 1.0 Hz, 1H), 7.66 – 7.59 (m, 3H), 7.44 – 7.40 (m, 2H), 5.56 (s, 2H). ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.38. ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.91, 166.85, 153.33, 151.18, 138.62, 130.44, 130.35 (q, 4.5 Hz) 130.21, 130.08, 129.91 (q, 32 Hz) 128.75 (q, 270 Hz) 126.76, 126.66 (q, 3.2 Hz) 115.42, 104.24, 69.81; HRMS (ESI): *m/z* calcd for $C_{18}H_{10}NO_2F_3I$ $[M+H]^+$; 455.9708, found: 455.9703.

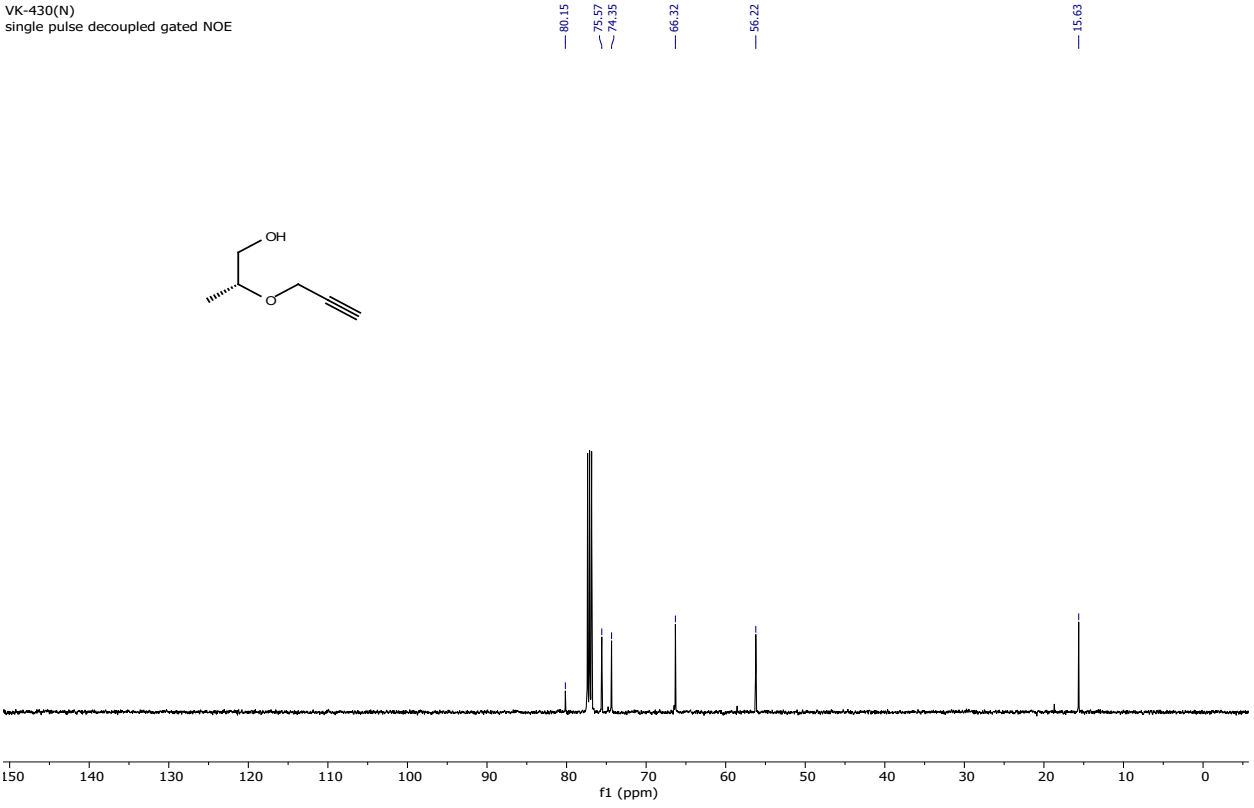
Compound S_{2b}, ^{1}H NMR, $CDCl_3$, 400 MHz

VK-430(N)
single_pulse



Compound S_{2b}, ^{13}C NMR, $CDCl_3$, 101 MHz

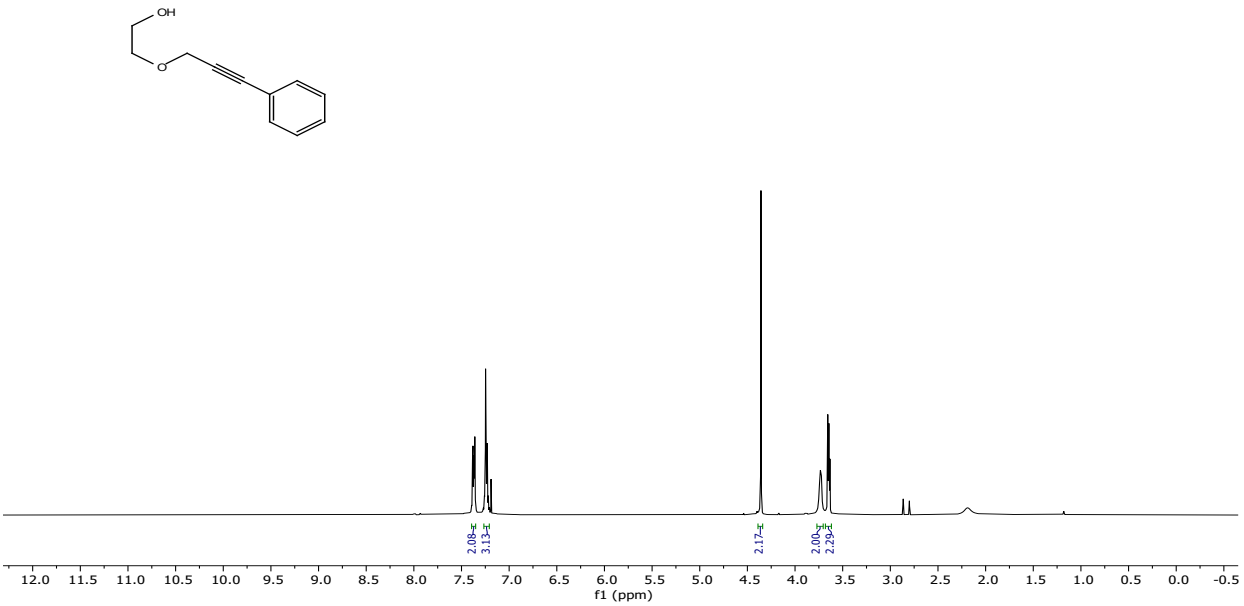
VK-430(N)
single pulse decoupled gated NOE



Spectral (^{1}H and ^{13}C) Data of Sonogashira Coupling Products (S_{3a-l}).

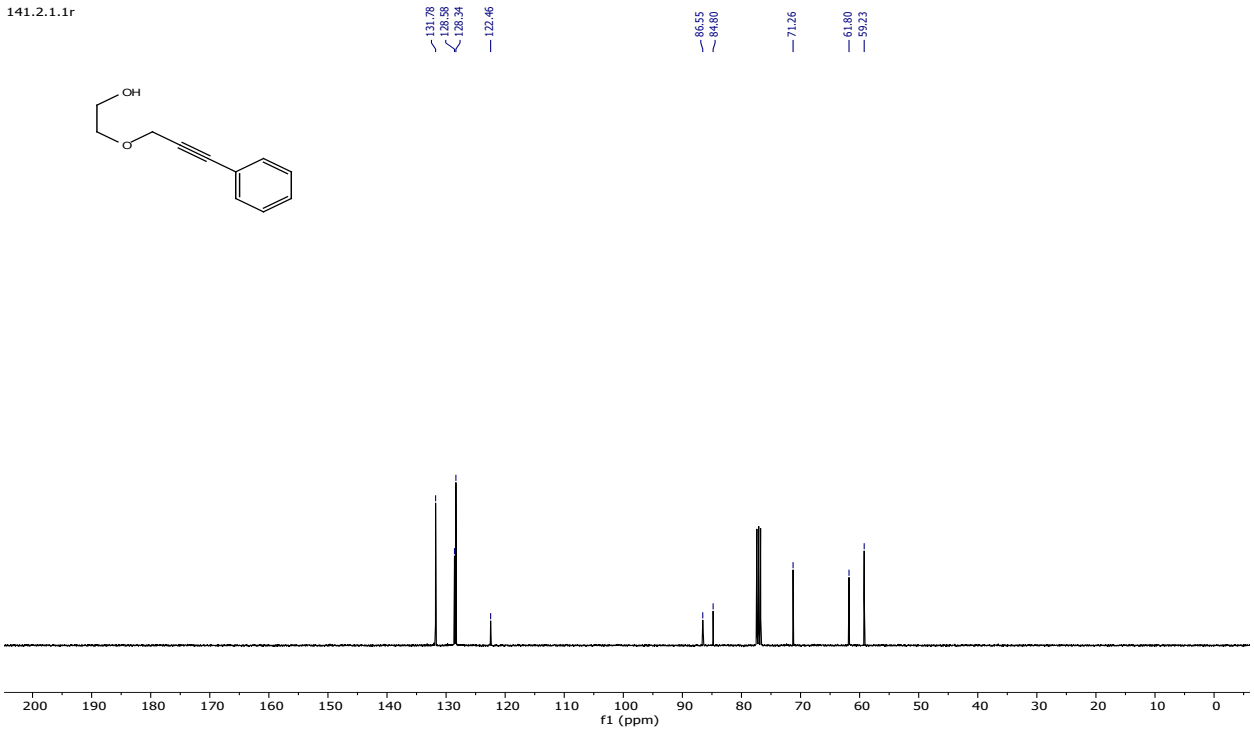
Compound S_{3a}, ^{1}H NMR, $CDCl_3$, 400 MHz

141.1.1.1r



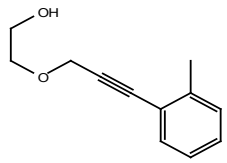
Compound S_{3a}, ^{13}C NMR, $CDCl_3$, 101 MHz

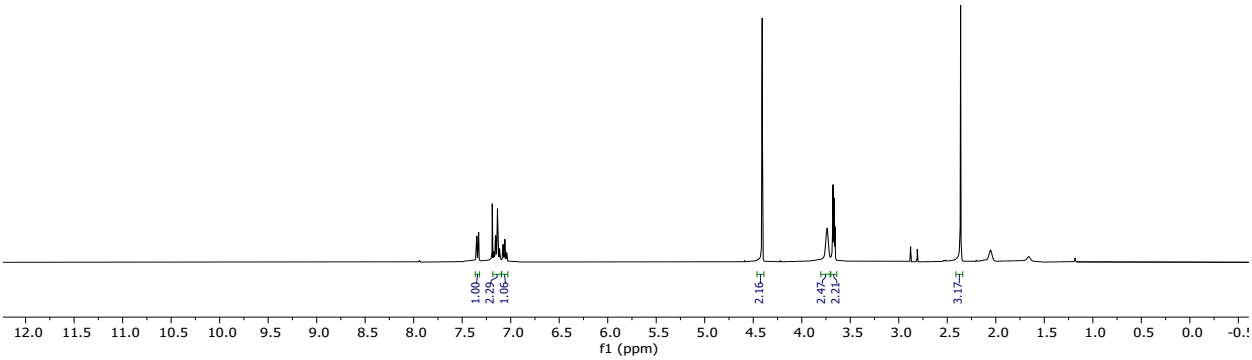
141.2.1.1r



Compound S_{3b}, ^{1}H NMR, $CDCl_3$, 400 MHz

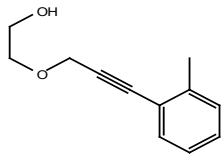
138 and 109.5.1.1r

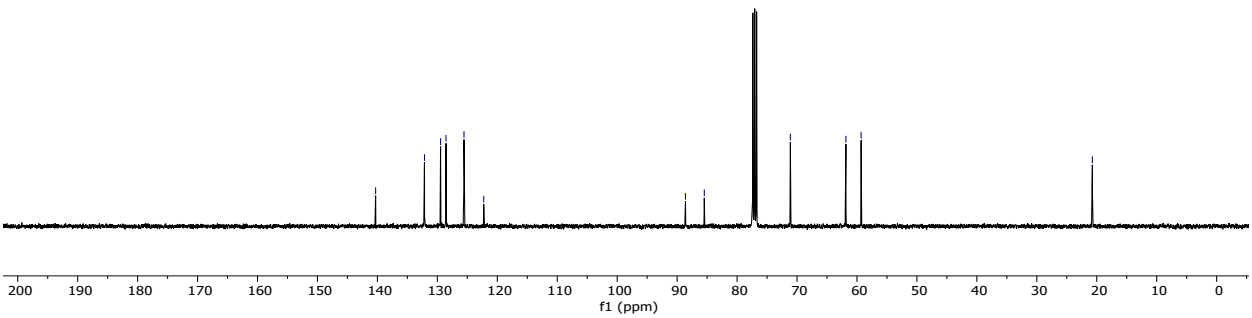




Compound S_{3b}, ^{13}C NMR, $CDCl_3$, 101 MHz

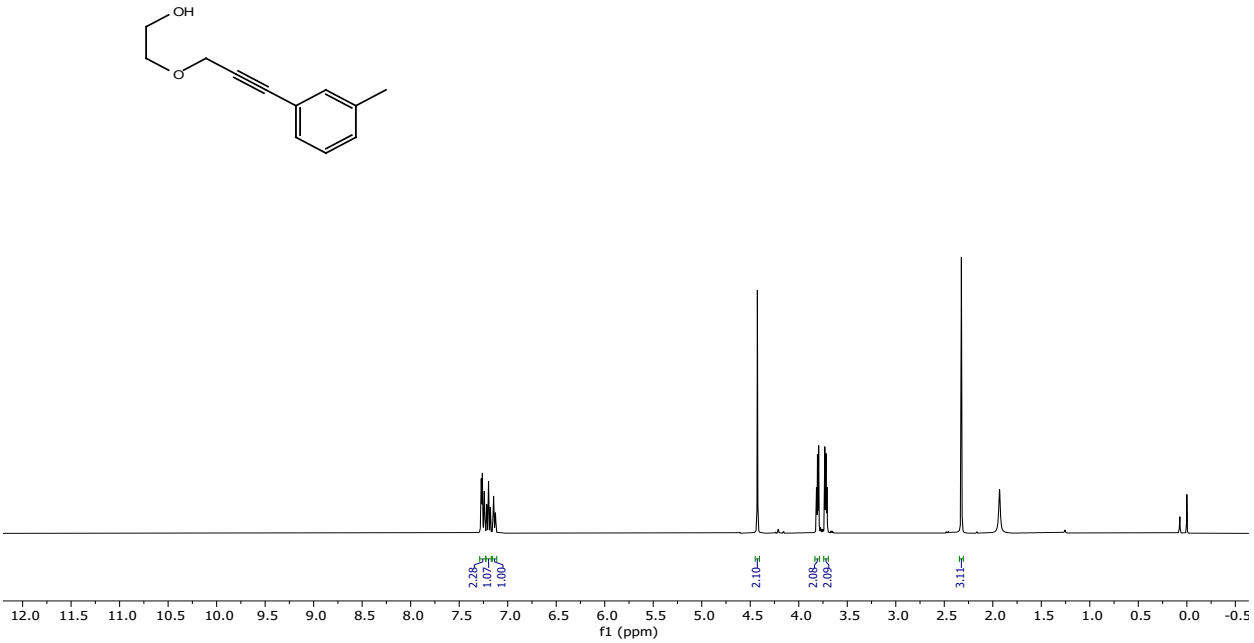
138 and 109.6.1.1r



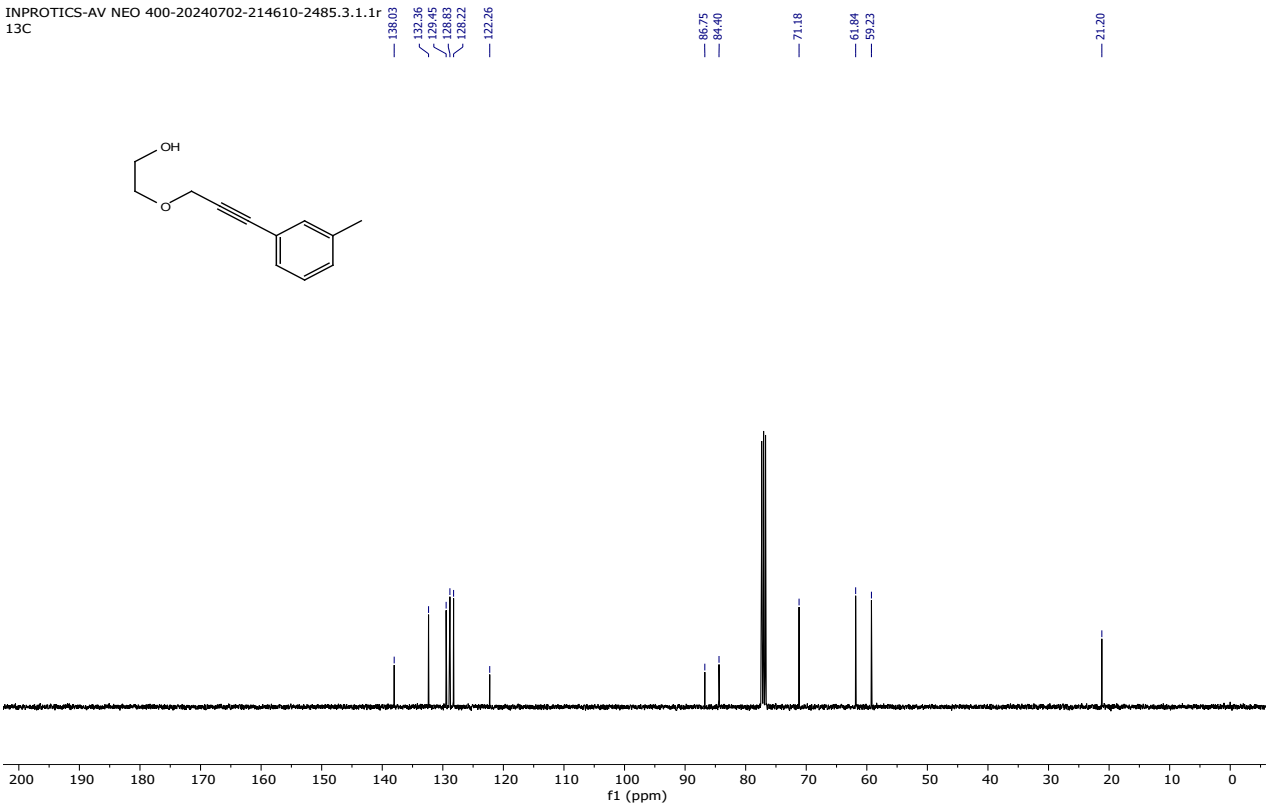


Compound S_{3c}, ^{1}H NMR, $CDCl_3$, 400 MHz

INPROTICS-AV NEO 400-20240702-214610-2485.1.1.1r
1H

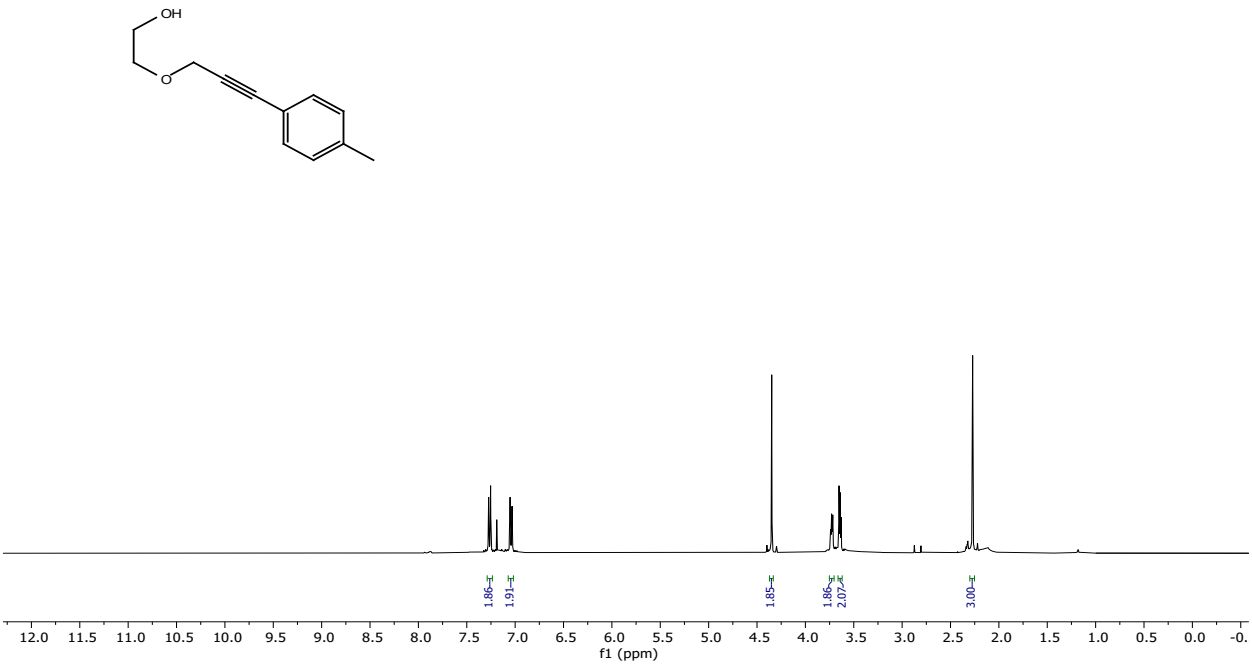


Compound S_{3c}, ^{13}C NMR, $CDCl_3$, 101 MHz



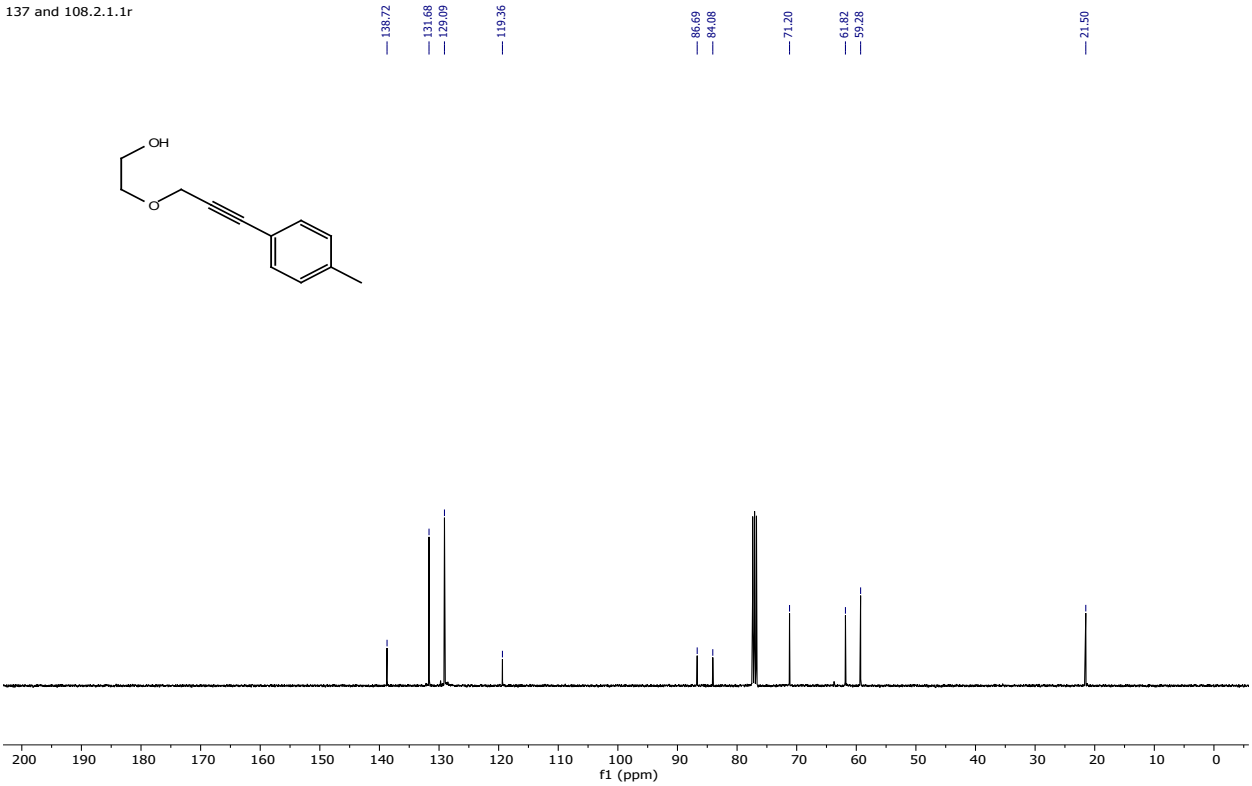
Compound S_{3d}, ^{1}H NMR, $CDCl_3$, 400 MHz

137 and 108.1.1.1r



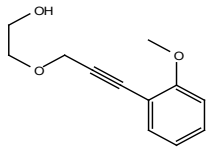
Compound S_{3d}, ^{13}C NMR, $CDCl_3$, 101 MHz

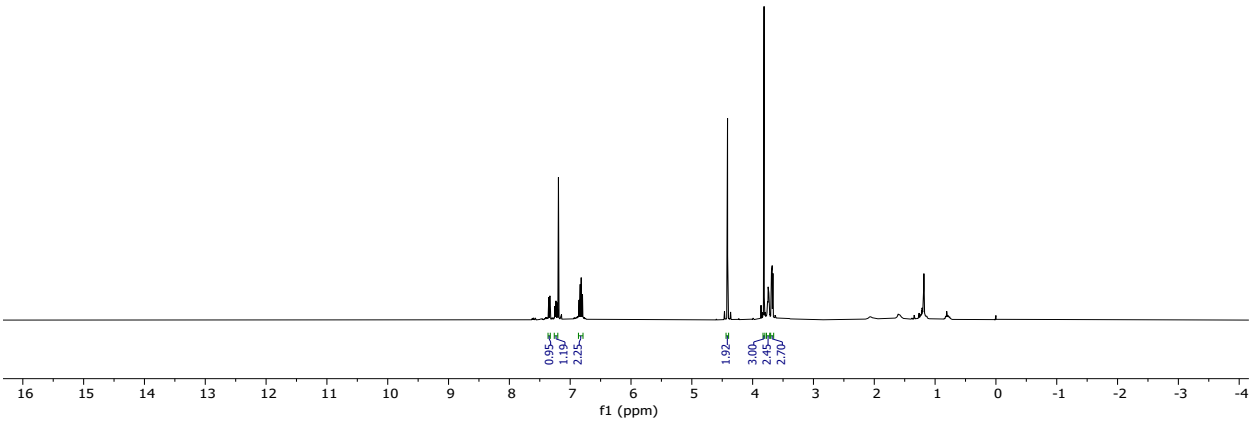
137 and 108.2.1.1r



Compound S_{3e}, ^{1}H NMR, $CDCl_3$, 400 MHz

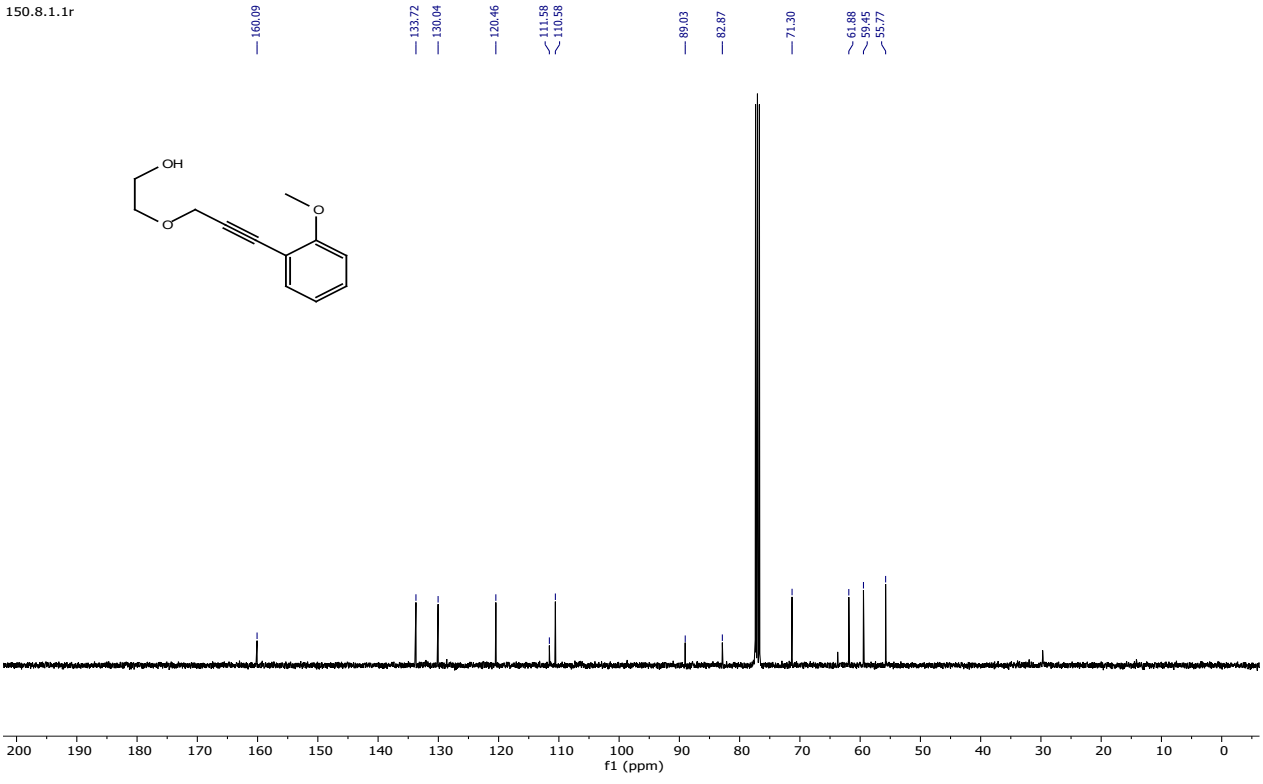
150.7.1.1r



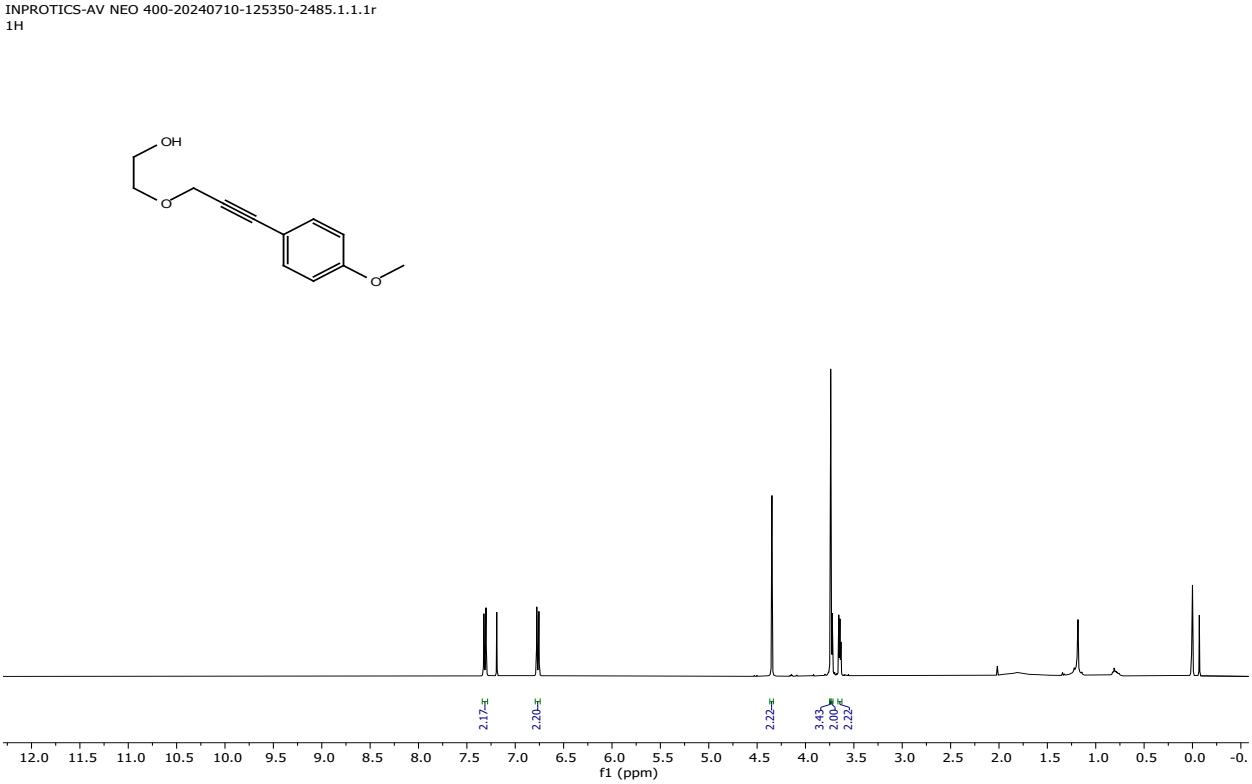


Compound S_{3e}, ^{13}C NMR, $CDCl_3$, 101 MHz

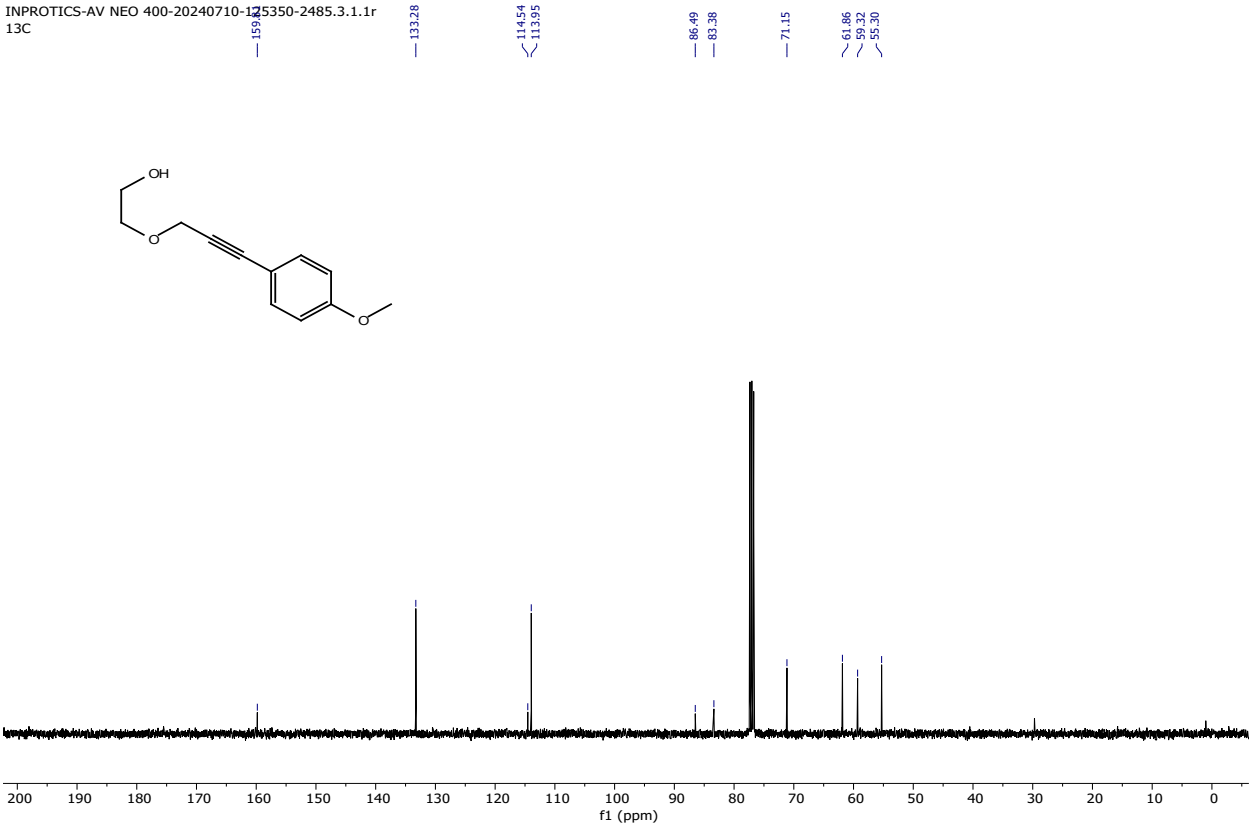
150.8.1.1r



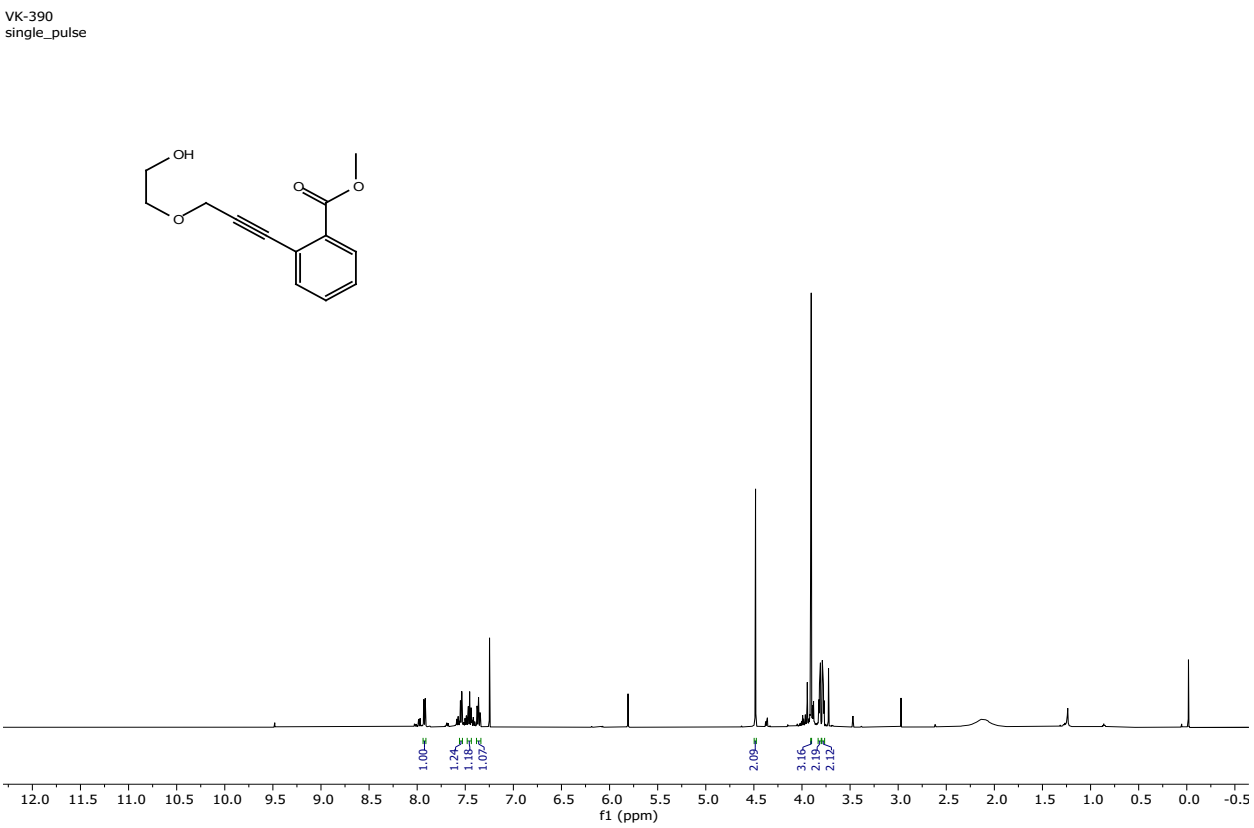
Compound S_{3f}, ^{1}H NMR, $CDCl_3$, 400 MHz



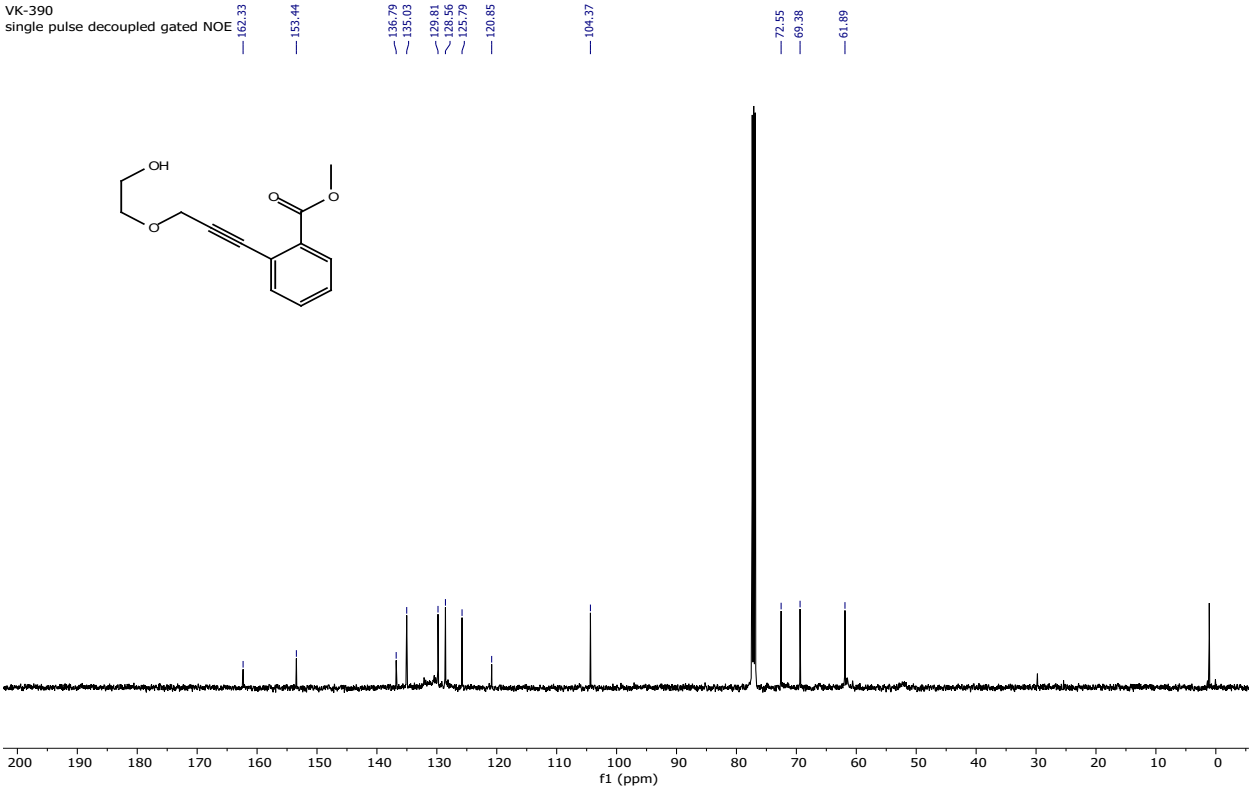
Compound S_{3f}, ^{13}C NMR, $CDCl_3$, 101 MHz



Compound S_{3g}, ^{1}H NMR, $CDCl_3$, 400 MHz

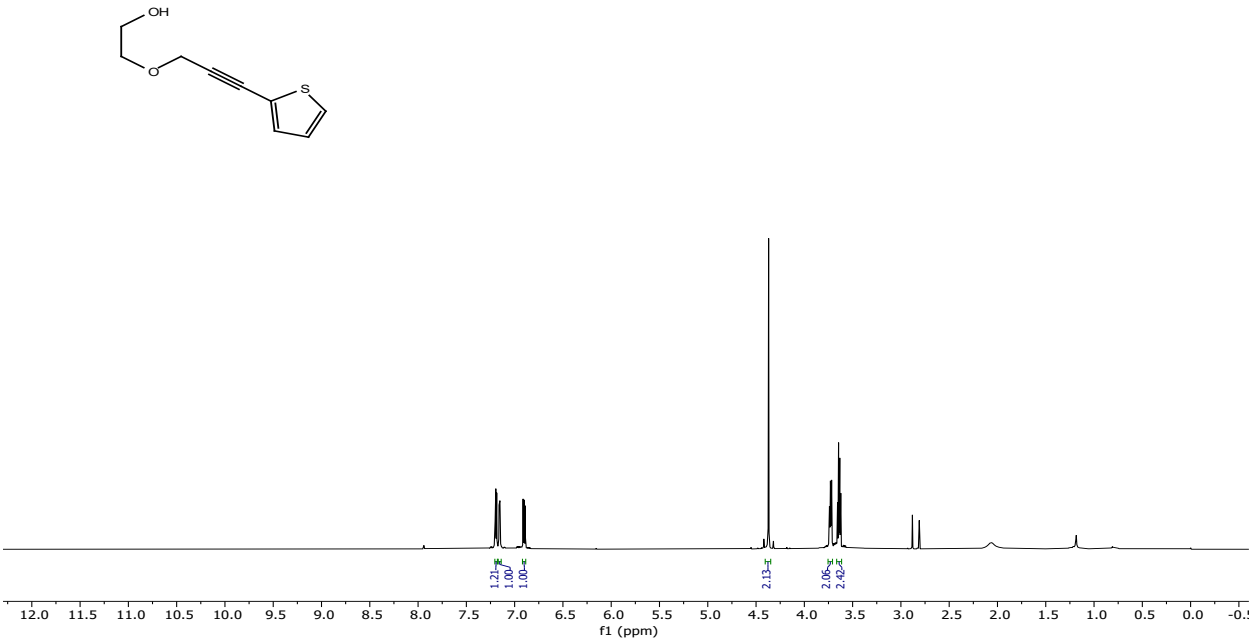


Compound S_{3g}, ^{13}C NMR, $CDCl_3$, 101 MHz



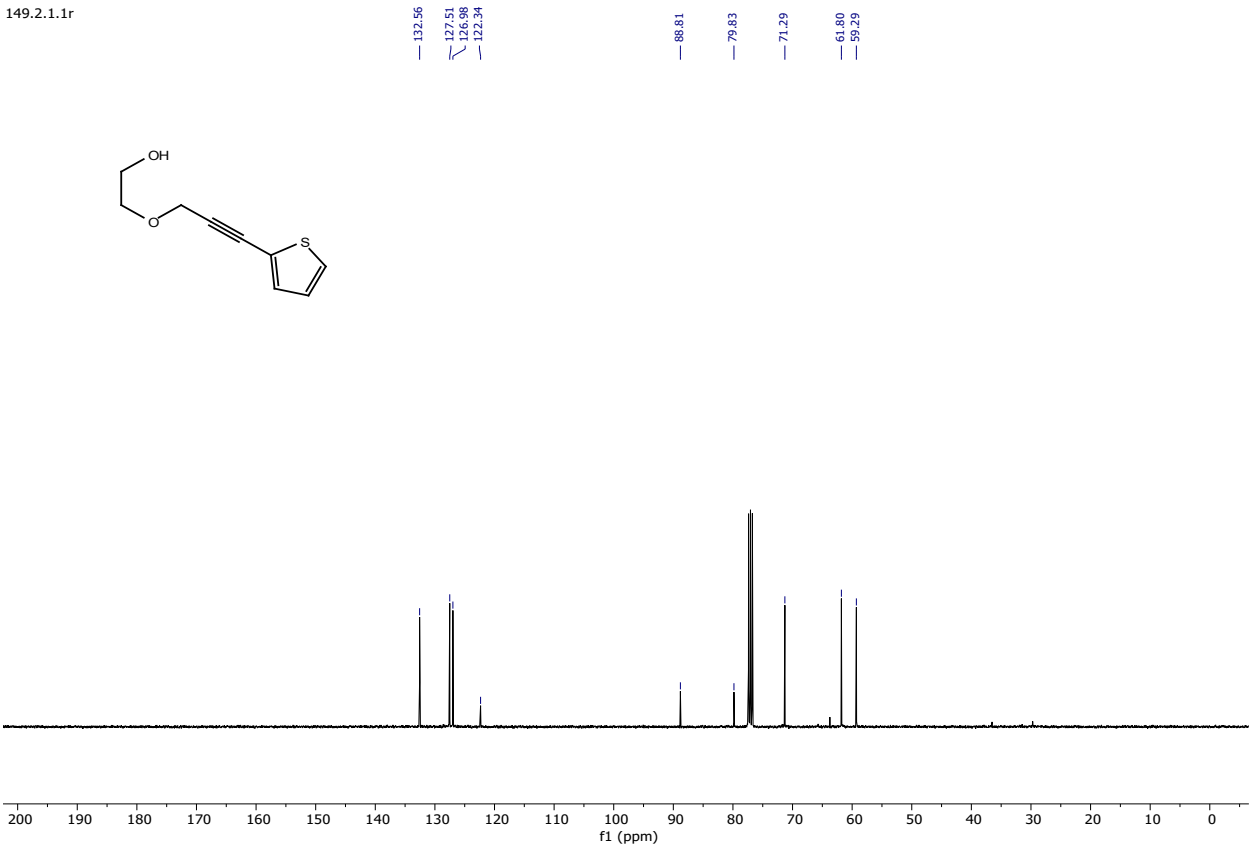
Compound S_{3h}, ^{1}H NMR, $CDCl_3$, 400 MHz

149.1.1.1r

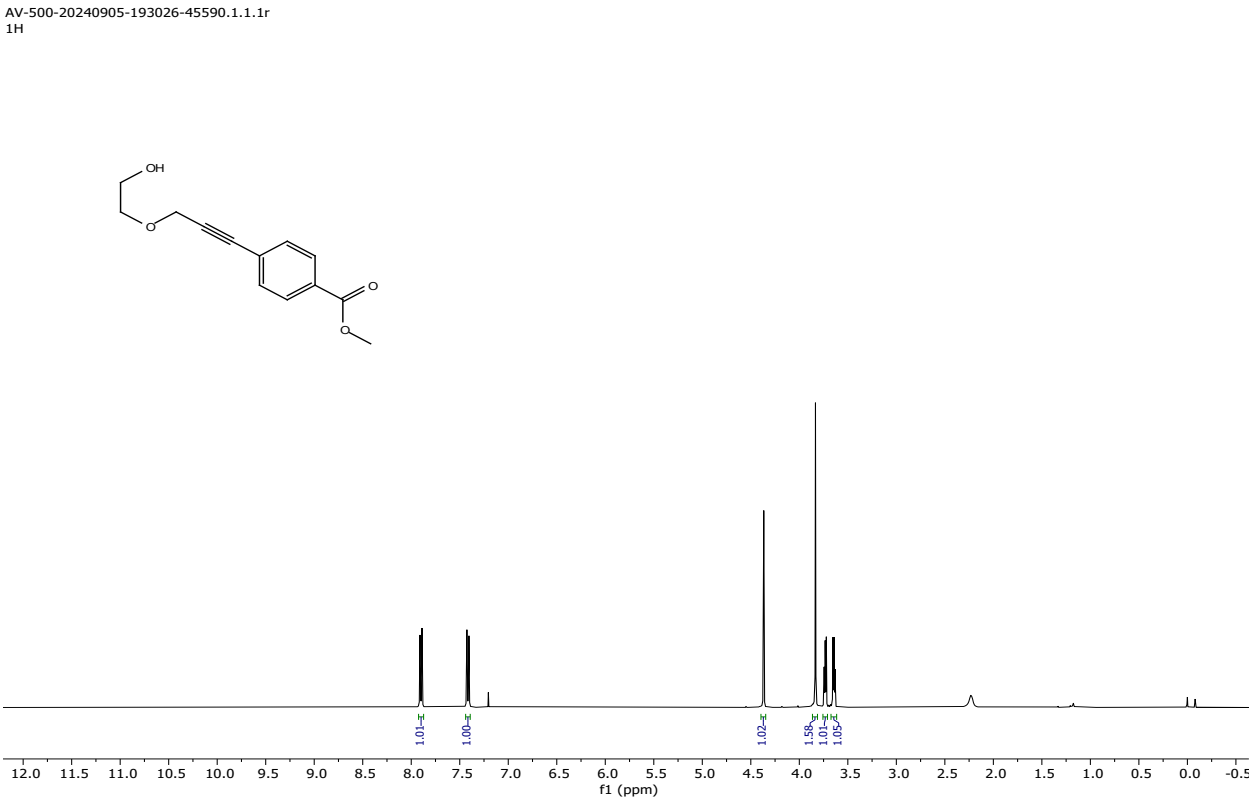


Compound S_{3h}, ^{13}C NMR, $CDCl_3$, 101 MHz

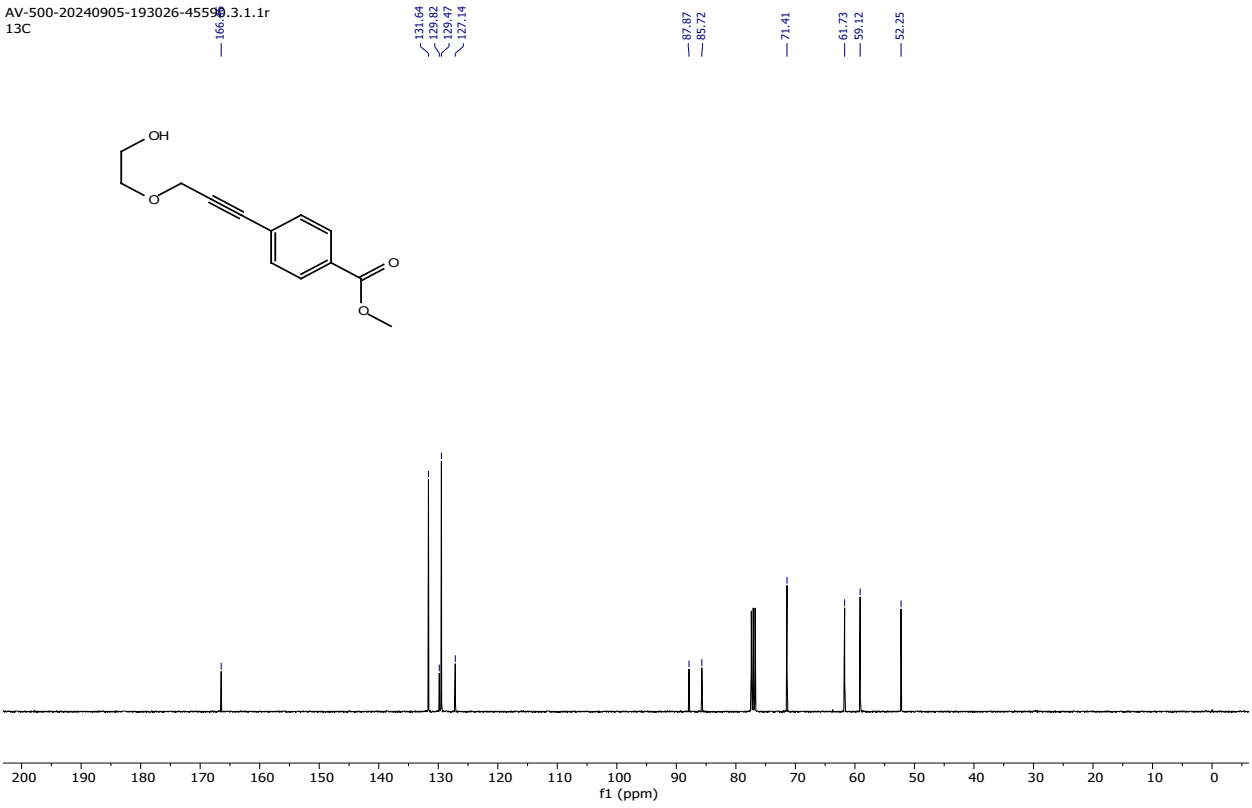
149.2.1.1r



Compound S_{3i}, ^{1}H NMR, $CDCl_3$, 400 MHz

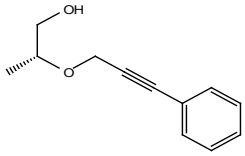


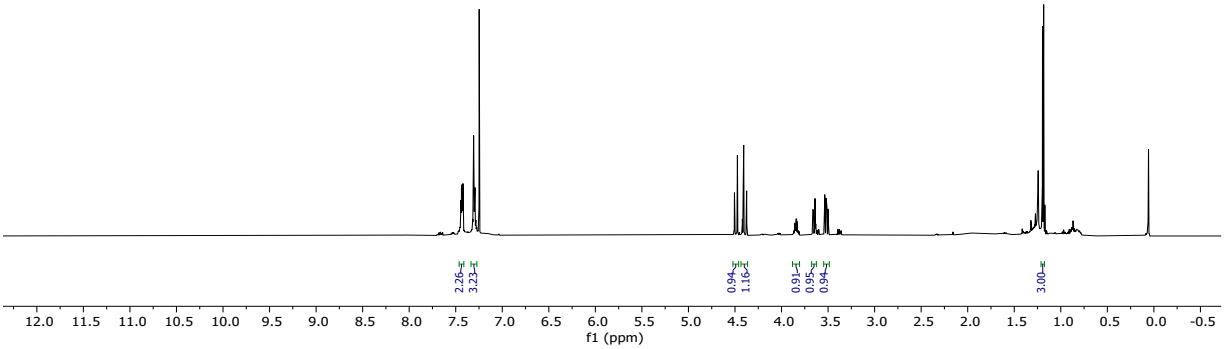
Compound S_{3i}, ^{13}C NMR, $CDCl_3$, 101MHz



Compound $S_{3j,}$ ^{1}HNMR, $CDCl_3$, 500 MHz

vk-438
single_pulse

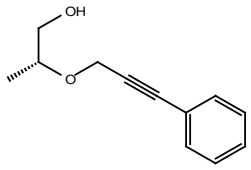


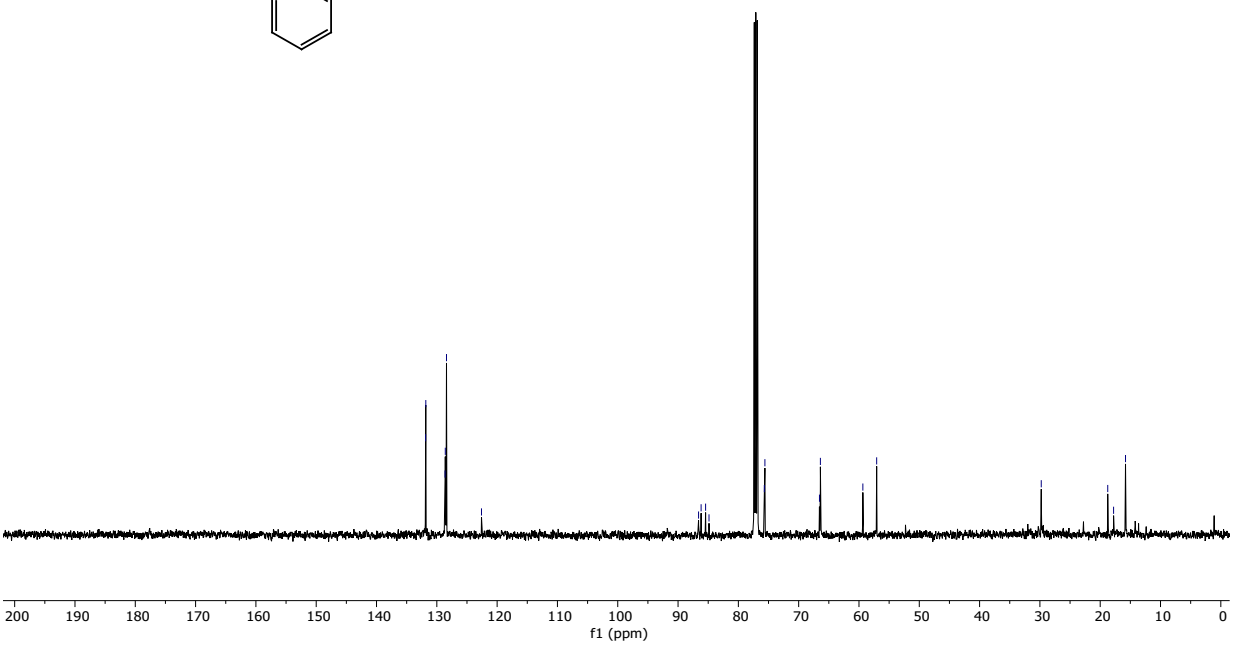


Compound S_{3j}, ^{13}C NMR, $CDCl_3$, 126 MHz

VK-438
single pulse decoupled gated NOE

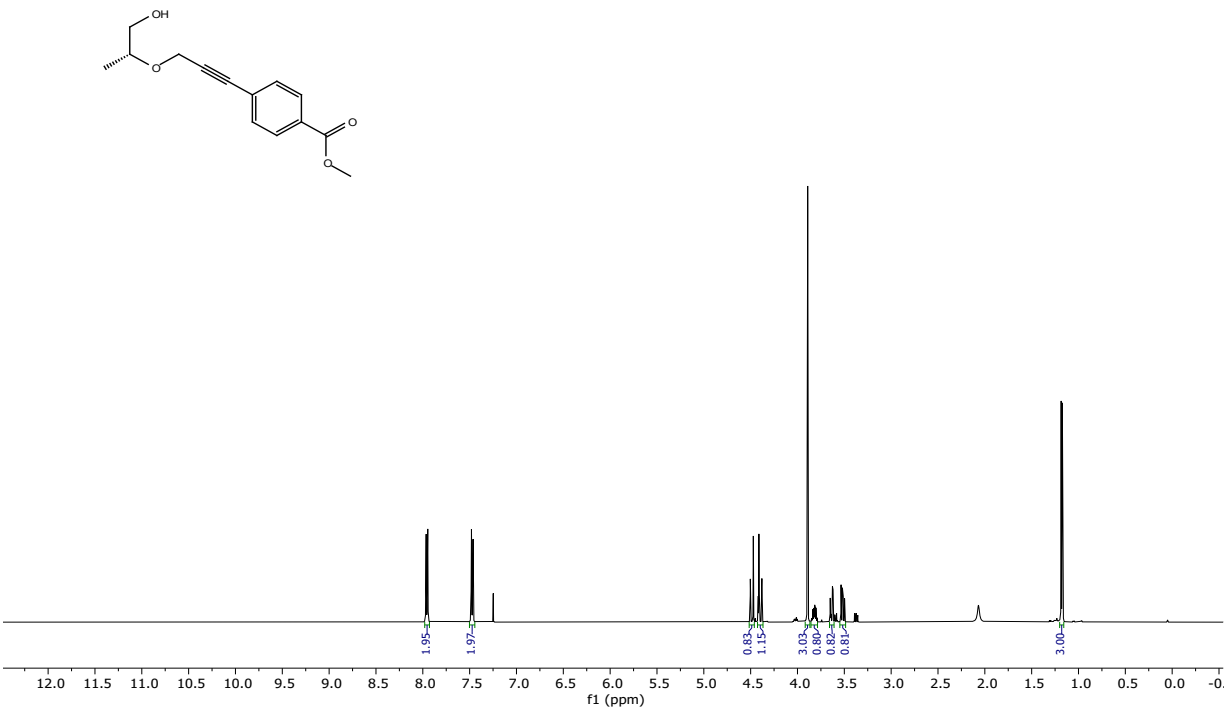
131.86
131.83
128.64
128.60
128.40
122.59
86.60
86.18
85.43
84.87
75.69
75.60
66.55
66.40
59.36
57.07
29.78
18.75
17.78
15.80





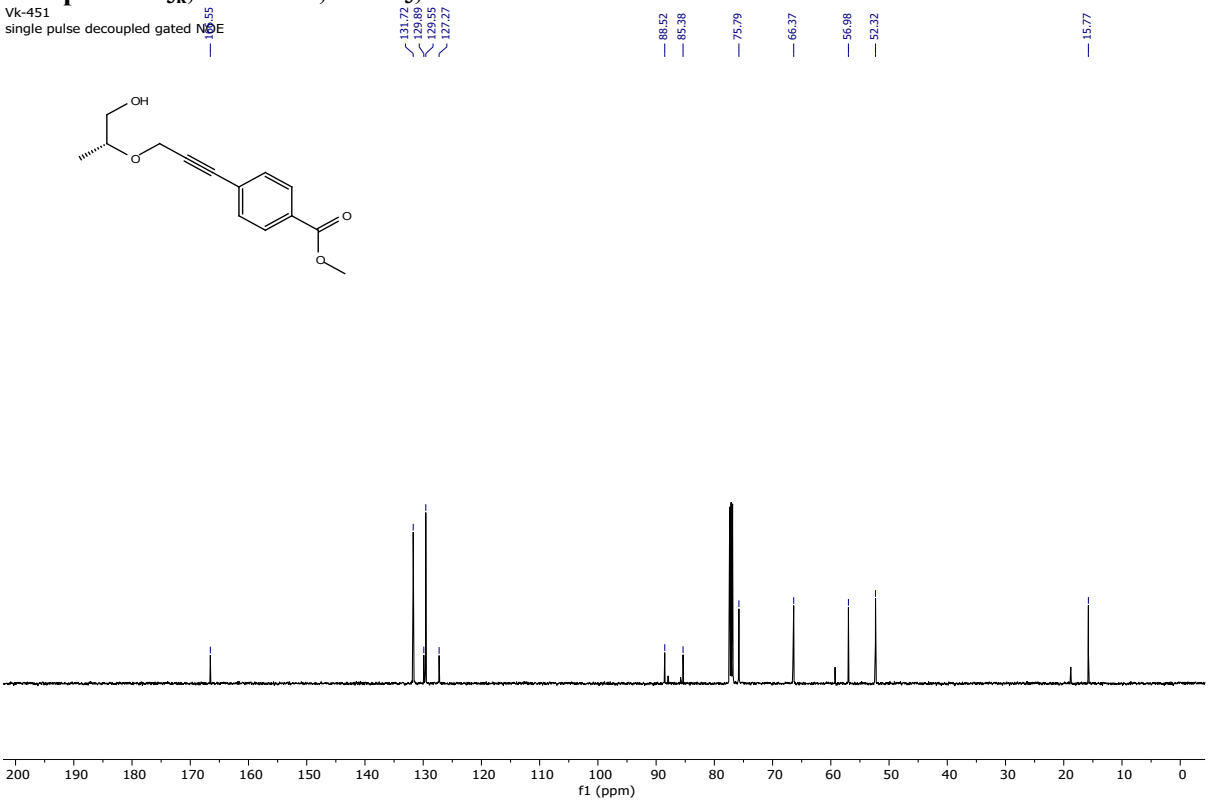
Compound S_{3k}, ^{1}H NMR, $CDCl_3$, 400 MHz

Vk-451
single_pulse



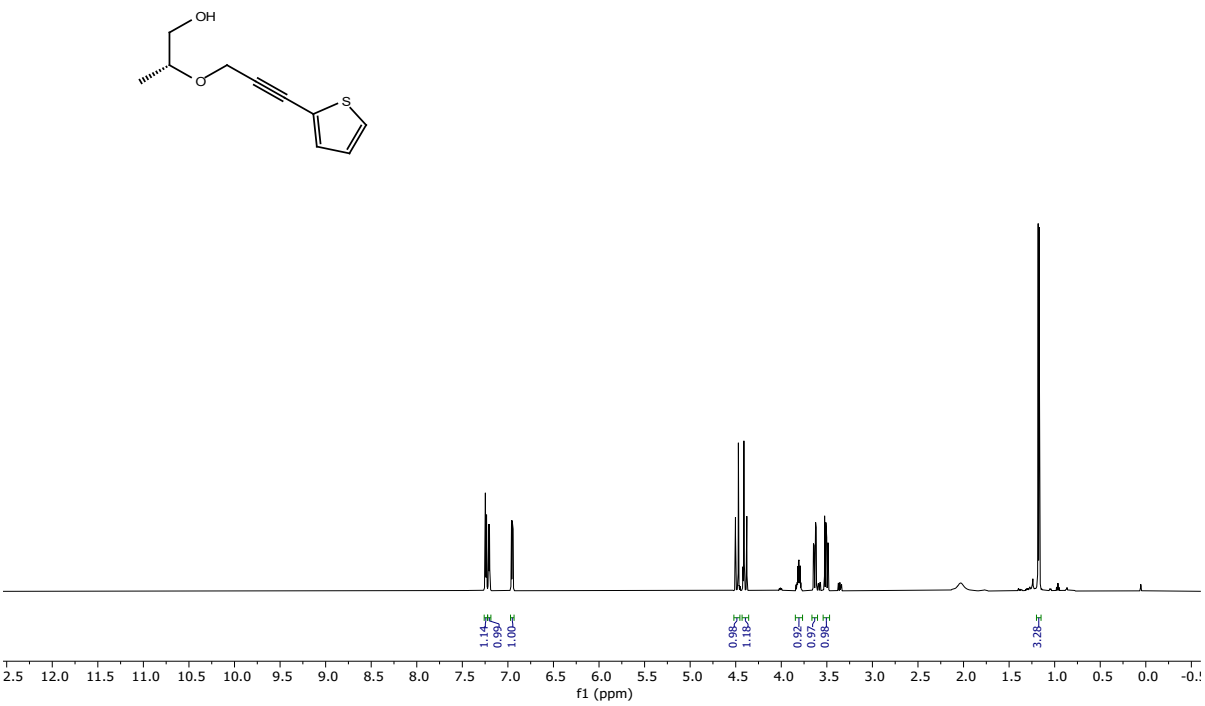
Compound S_{3k}, ^{13}C NMR, $CDCl_3$, 101MHz

Vk-451
single pulse decoupled gated NOE



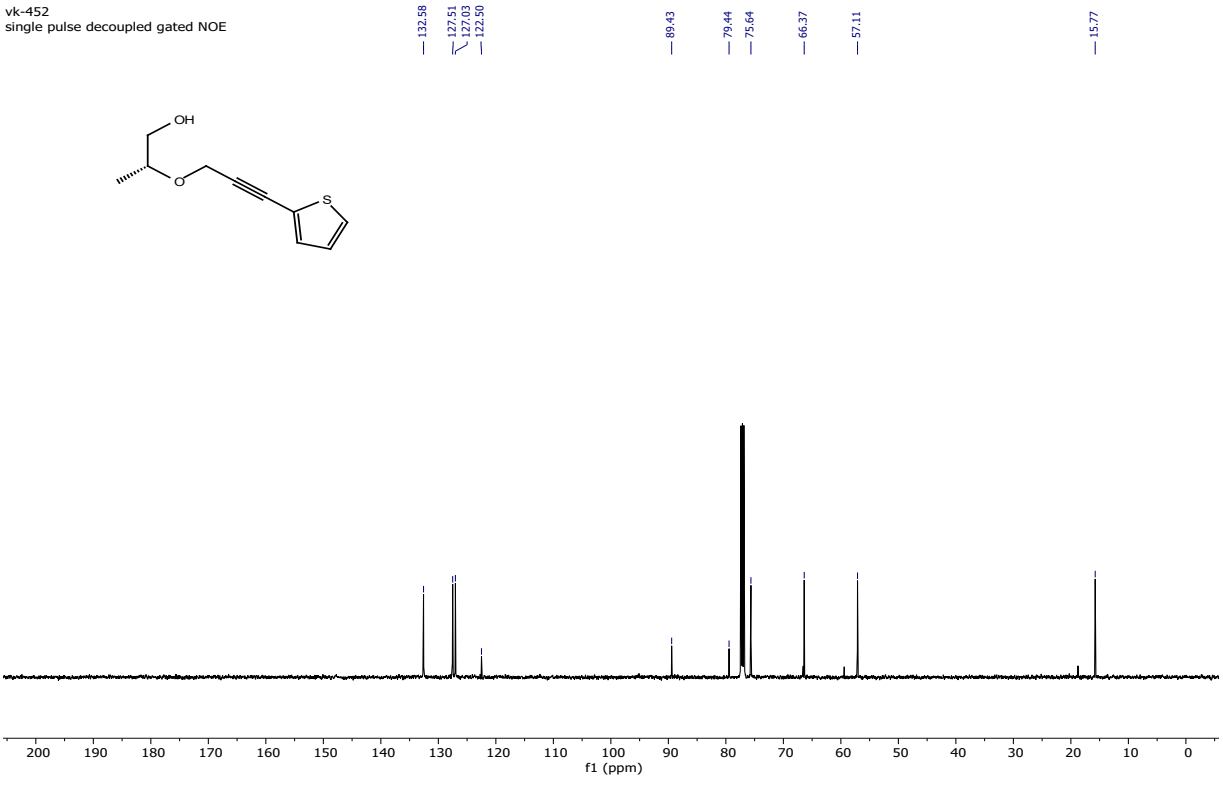
Compound S_{3l}, ^{1}H NMR, $CDCl_3$, 500 MHz

vk-452
single_pulse



Compound S_{3l}, ^{13}C NMR, $CDCl_3$, 126MHz

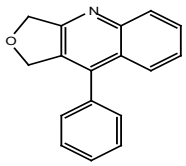
vk-452
single pulse decoupled gated NOE

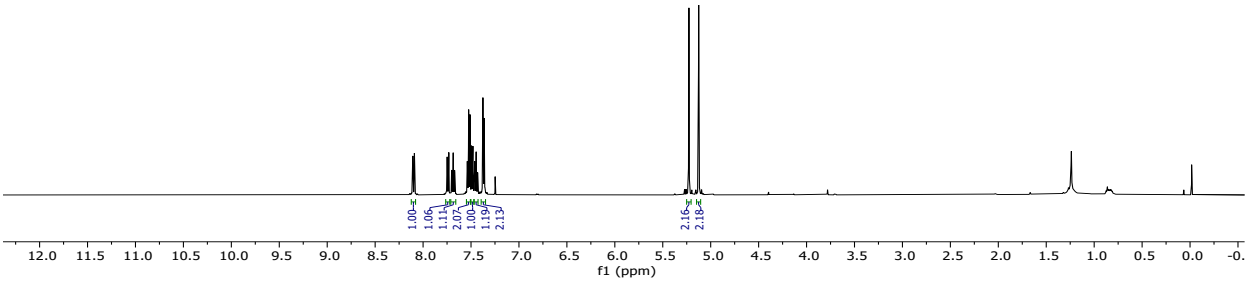


Spectral (^{1}H, ^{13}C and ^{19}F) Data of Dihydrofuroquinolines (3a-v)

Compound 3a, ^{1}H NMR, $CDCl_3$, 500 MHz

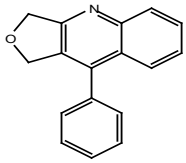
vk-165(D)
single_pulse

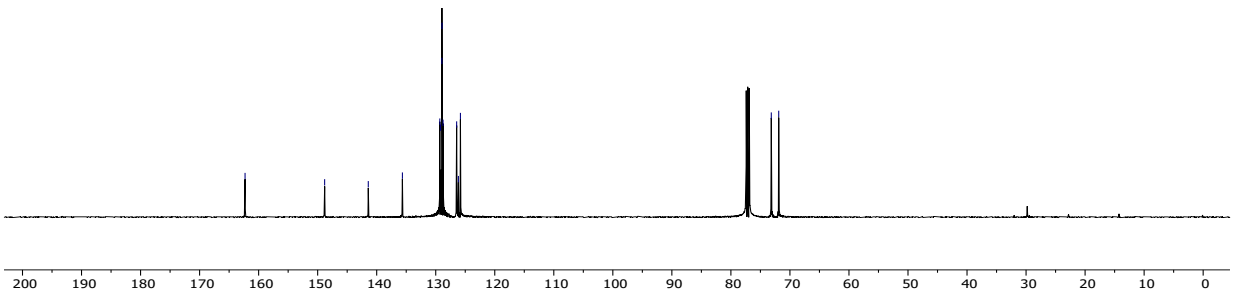




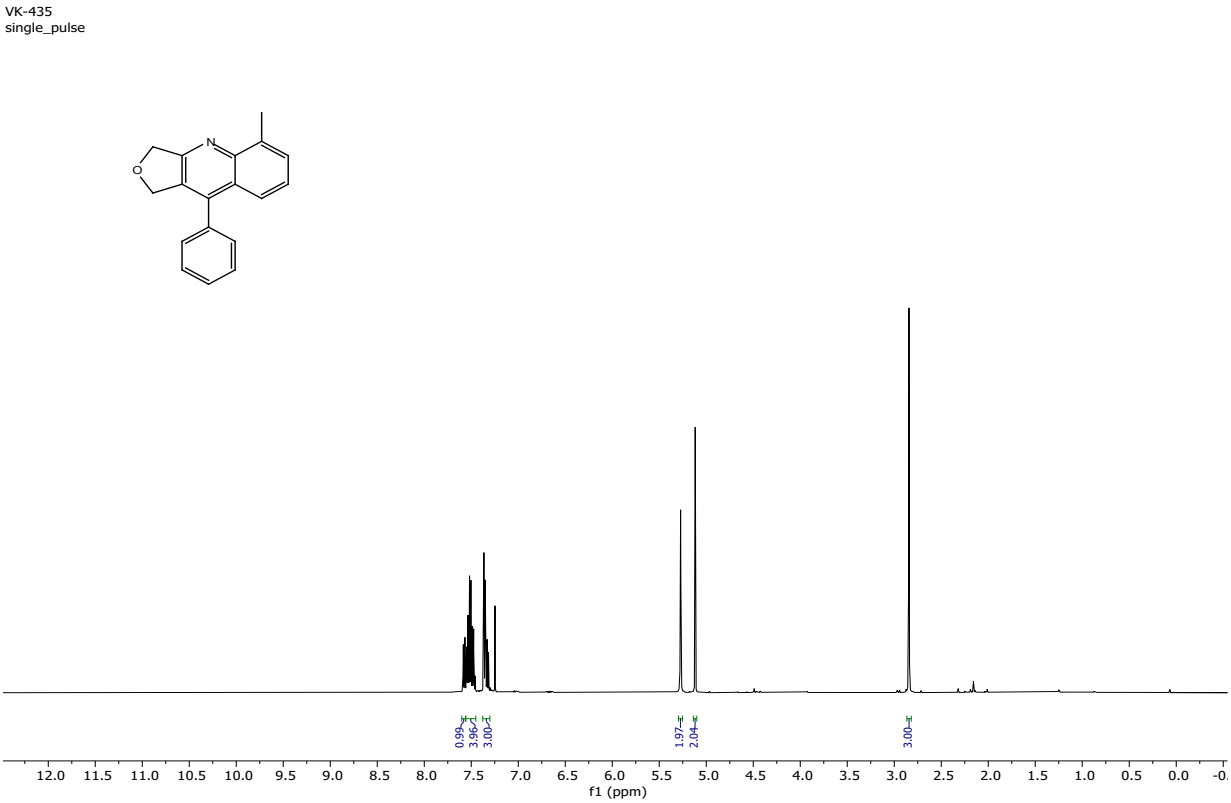
Compound 3a, ^{13}C NMR, $CDCl_3$, 126 MHz

VK-165(D)
single pulse decoupled gated NOE

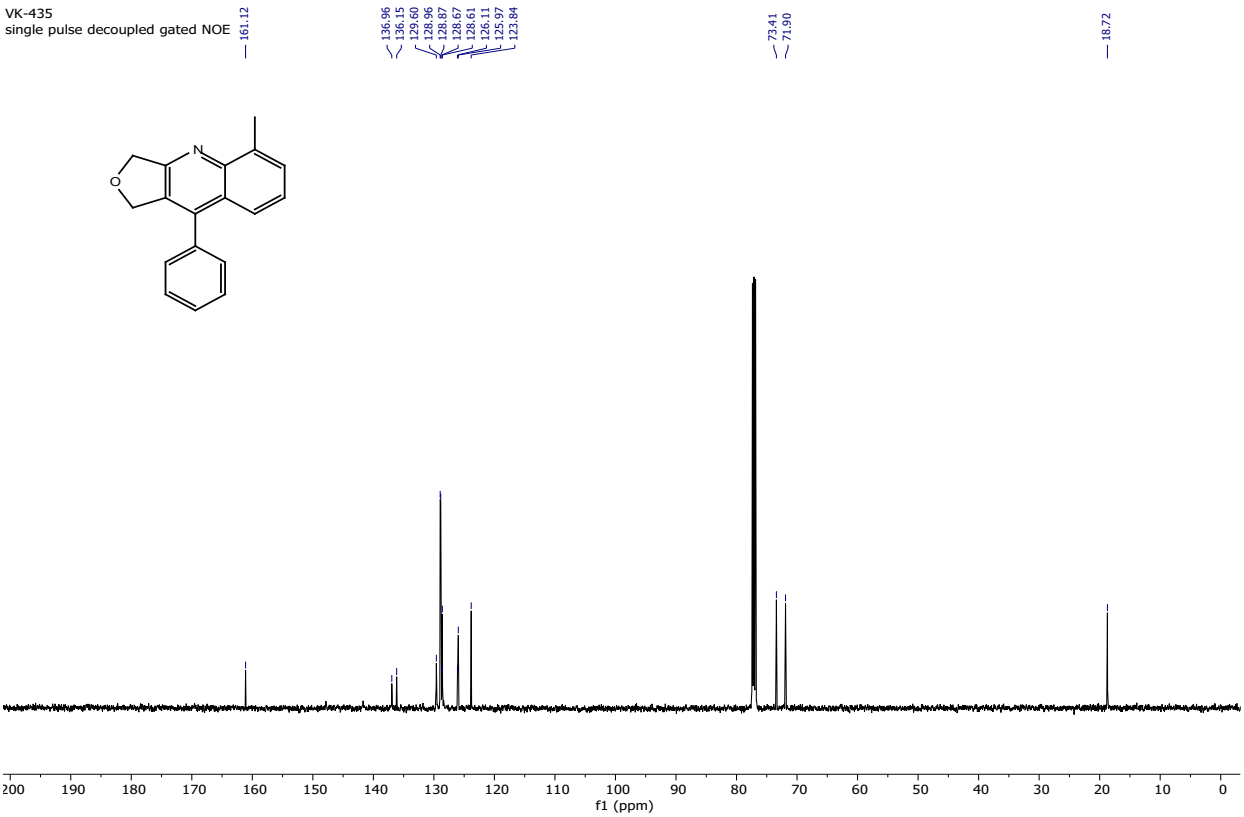




Compound 3b, ^{1}H NMR, $CDCl_3$, 500 MHz

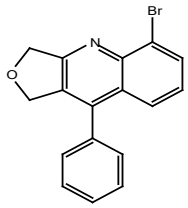


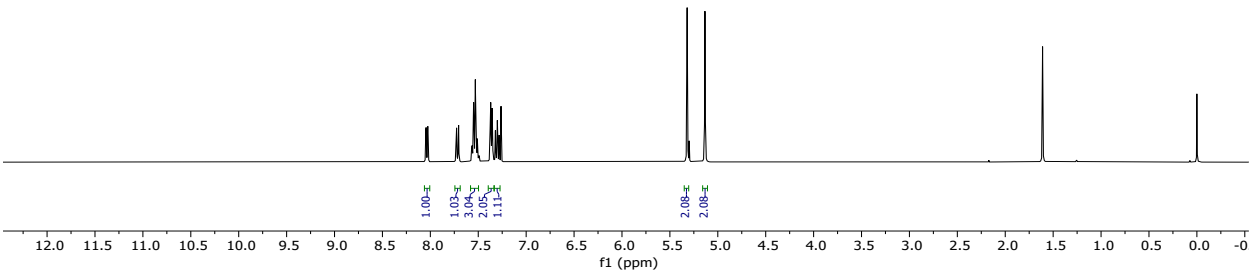
Compound 3b, ^{13}C NMR, $CDCl_3$, 126 MHz



Compound 3c, ^{1}H NMR, $CDCl_3$, 400 MHz

EXT40524.60.1.1r
Signature SIF VIT VELLORE
CUSBVK177

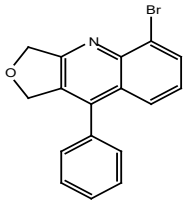


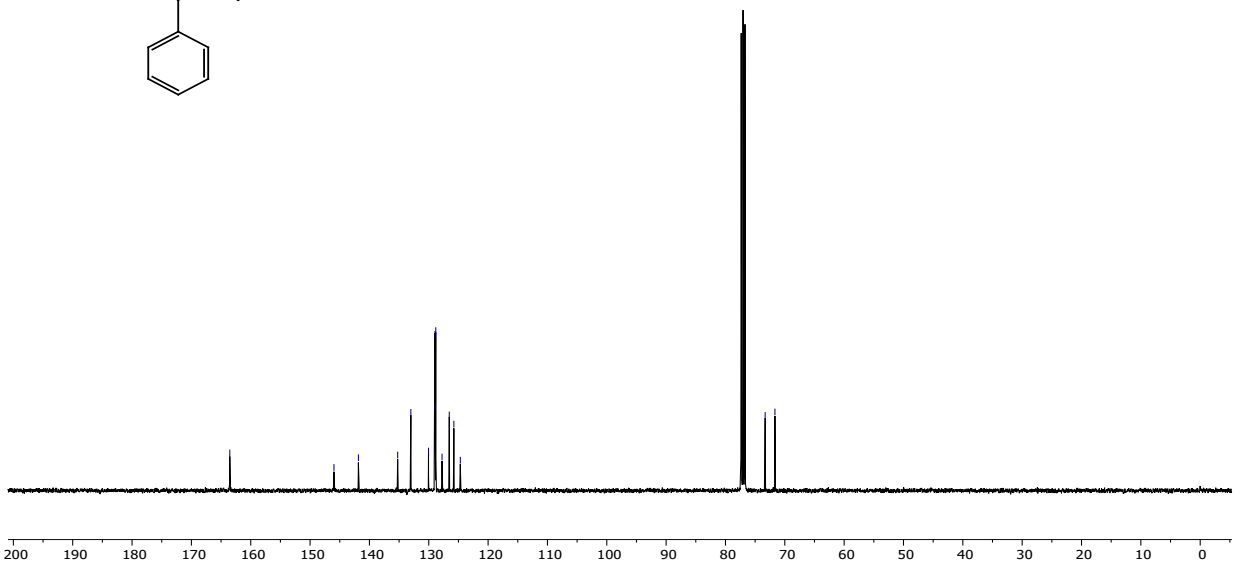


Compound 3c, ^{13}C NMR, $CDCl_3$, 101 MHz

EXT40524
Signature SIF VIT VELLORE
CUSBVK177

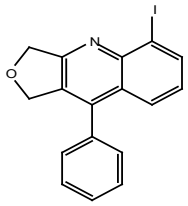
163.53
145.97
141.86
135.24
133.02
130.04
128.96
128.90
128.82
127.76
126.54
125.77
124.68
73.31
71.66

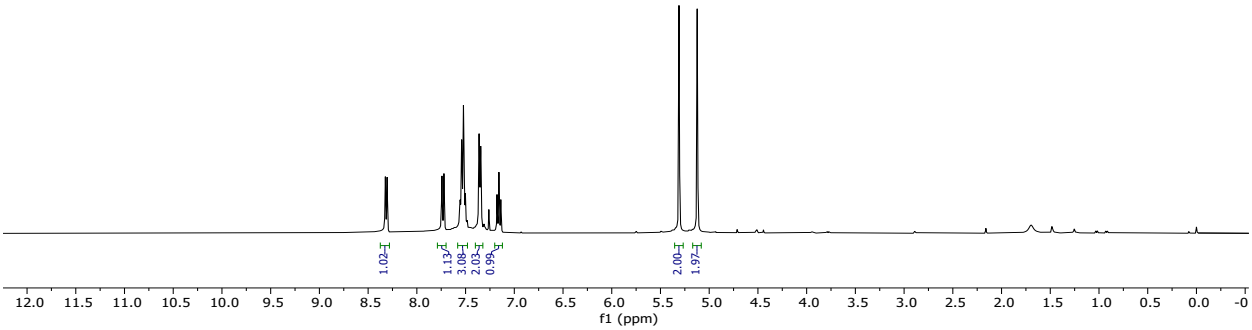




Compound 3d, ^{1}H NMR, $CDCl_3$, 400 MHz

EXT40524.90.1.1r
Signature SIF VIT VELLORE
CUSBVK171

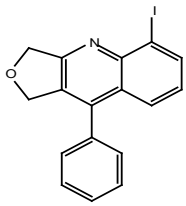


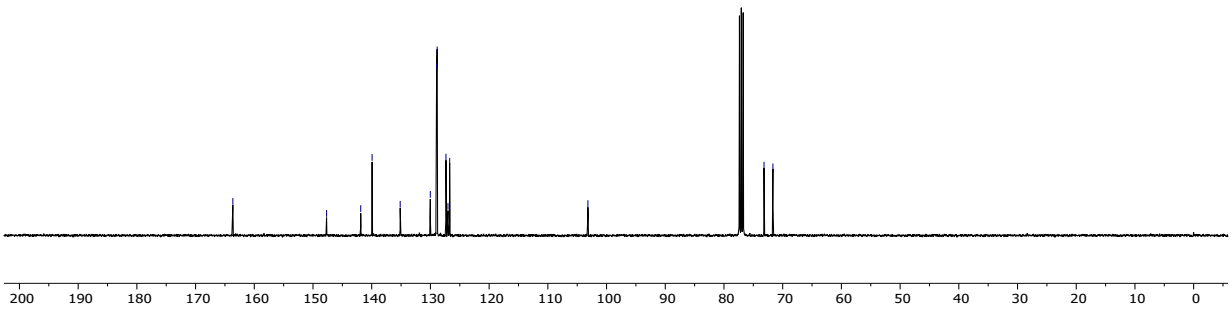


Compound 3d, ^{13}C NMR, $CDCl_3$, 101 MHz

EXT40524
Signature SIF VIT VELLORE
CUSBVK171

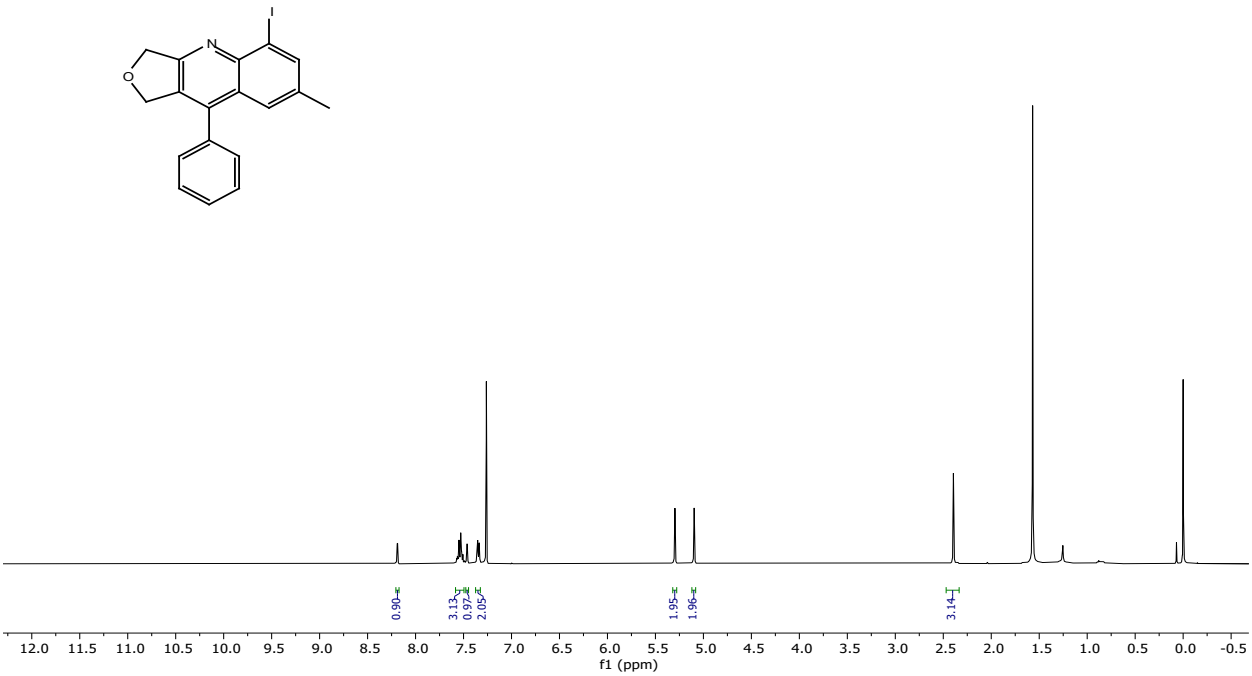
163.65
147.69
141.87
139.93
135.15
130.02
128.95
128.85
127.35
127.01
126.72
103.18
73.18
71.67





Compound 3e, ^{1}H NMR, $CDCl_3$, 500 MHz

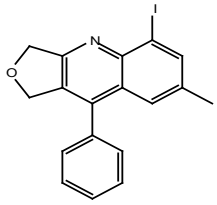
EXT40524.93.1.1r
Signature SIF VIT VELLORE
CUSBVK172

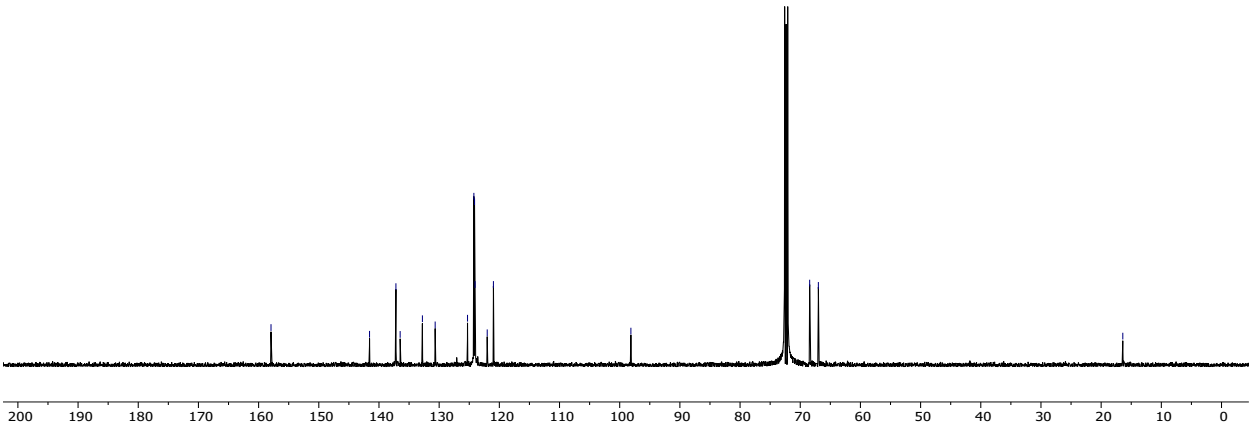


Compound 3e, ^{13}C NMR, $CDCl_3$, 126 MHz

vk-172
single pulse decoupled gated NOE

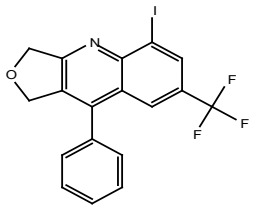
157.94
141.57
137.19
136.48
132.78
130.66
125.29
124.23
124.13
124.03
122.01
120.98
98.14
68.44
66.99
16.40

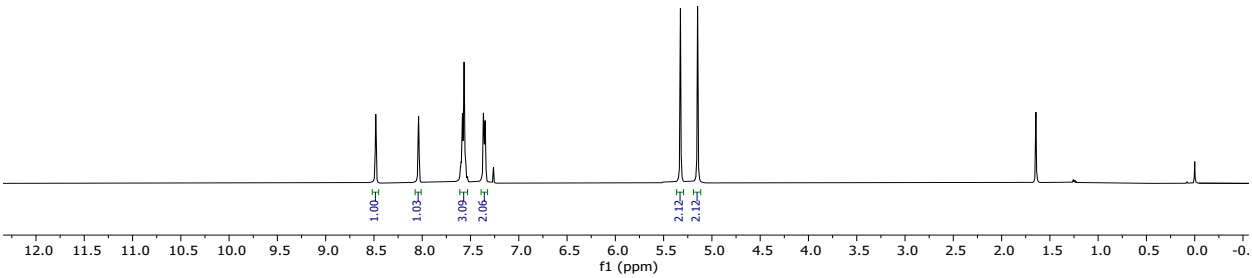




Compound 3f, ^{1}H NMR, $CDCl_3$, 400 MHz

EXT40524.27.1.1r
Signature SIF VIT VELLORE
CUSBVK173

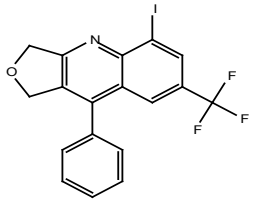


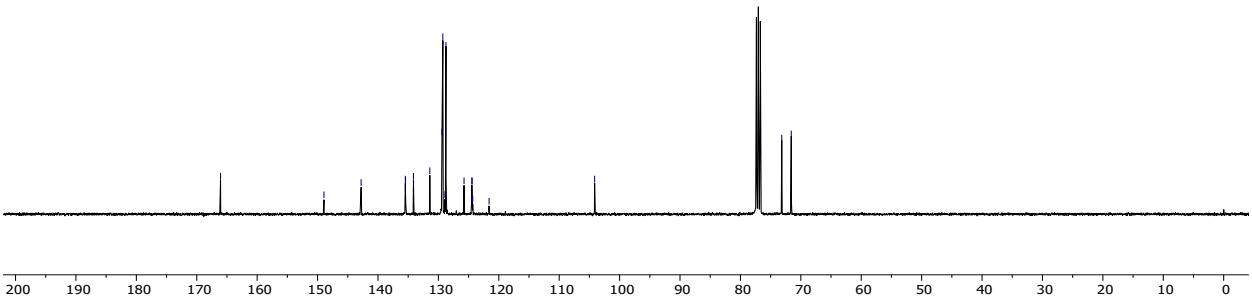


Compound 3f, ^{13}C NMR, $CDCl_3$, 101 MHz

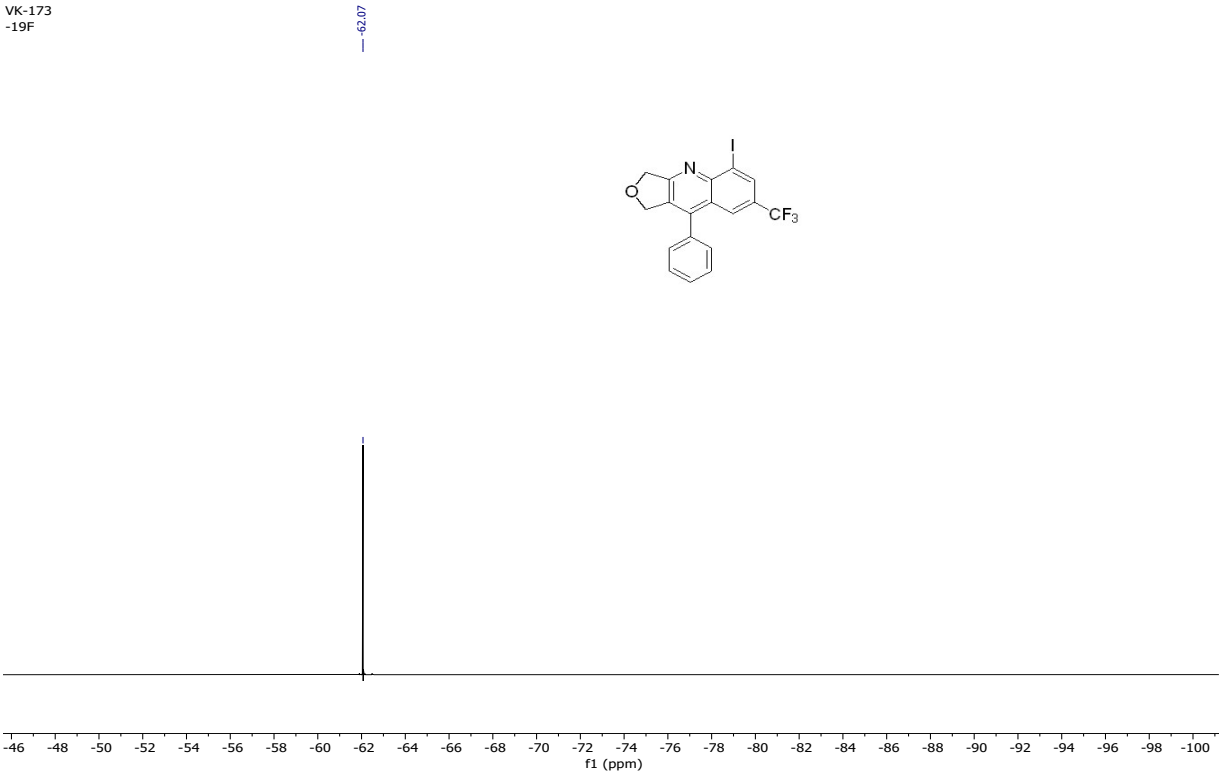
EXT40524
Signature SIF VIT VELLORE
CUSBVK173

166.06
148.94
142.79
135.47
135.44
134.13
131.42
129.41
129.26
128.91
128.75
125.75
124.50
124.46
124.42
124.37
124.32
121.61
104.14
73.16
71.58



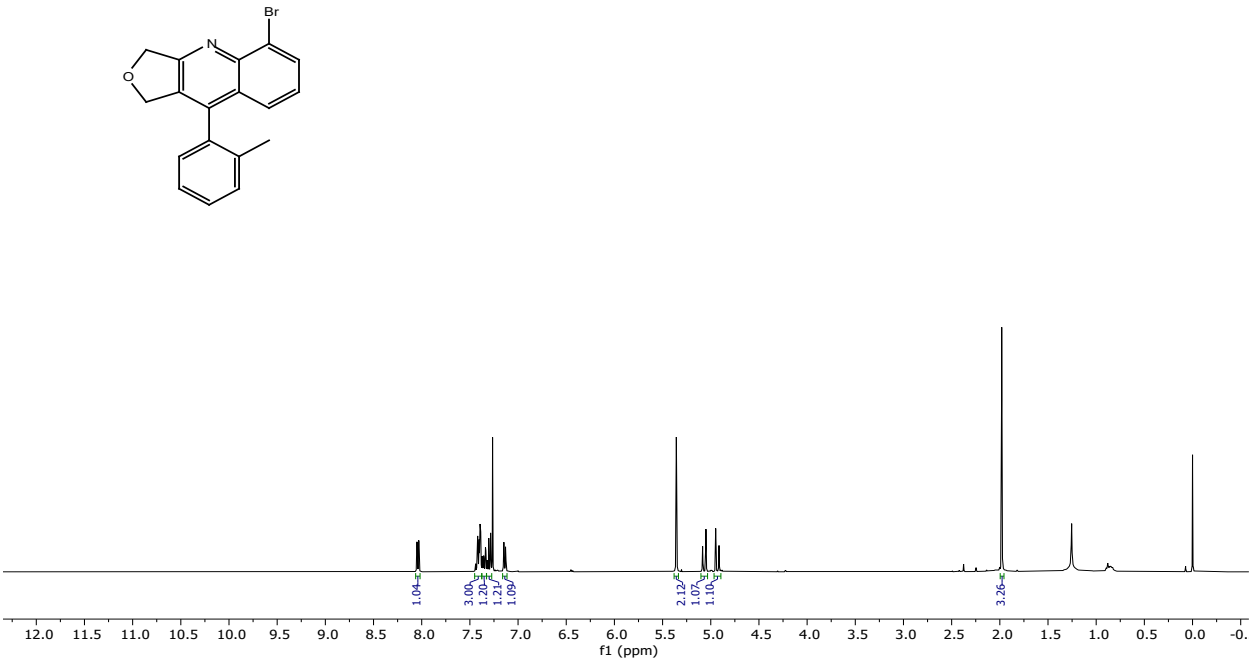


Compound 3f, ^{19}F NMR, $CDCl_3$, 471 MHz



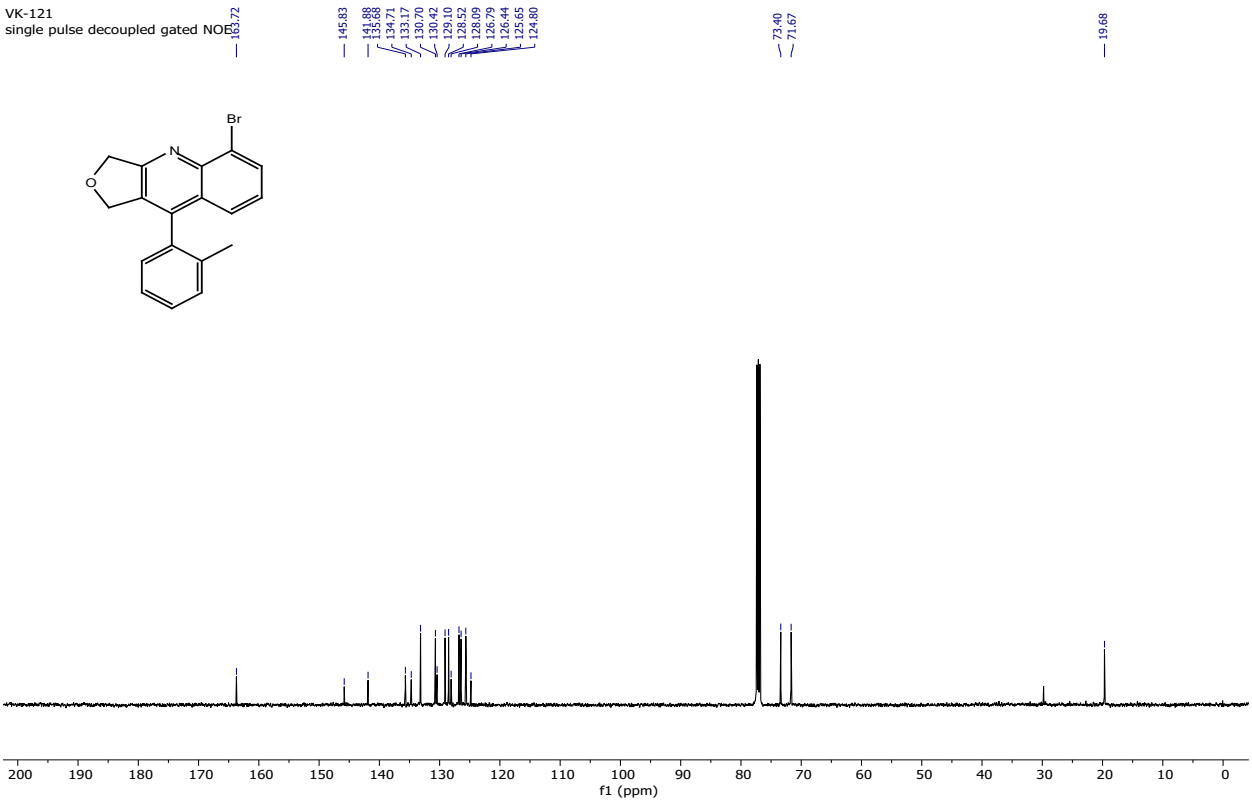
Compound 3g, ^{1}H NMR, $CDCl_3$, 400 MHz

CUSB-VK-121.10.1.1r
CUSB-VK-121



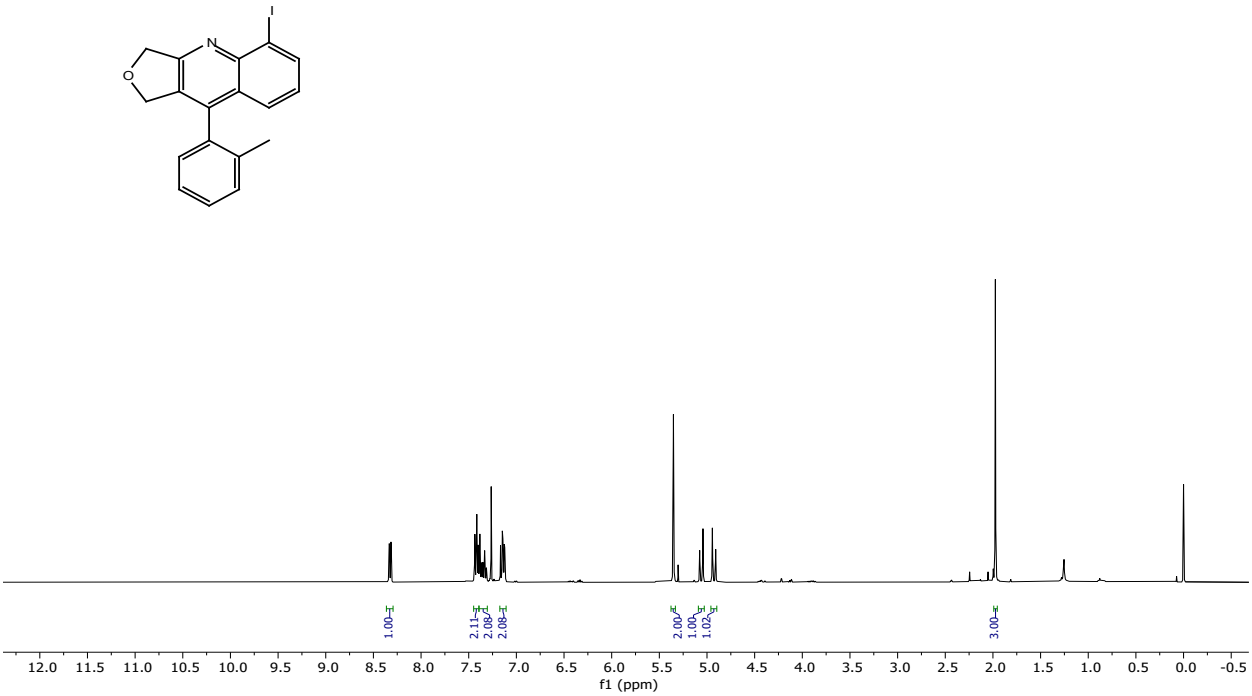
Compound 3g, ^{13}C NMR, $CDCl_3$, 101 MHz

VK-121
single pulse decoupled gated NOE



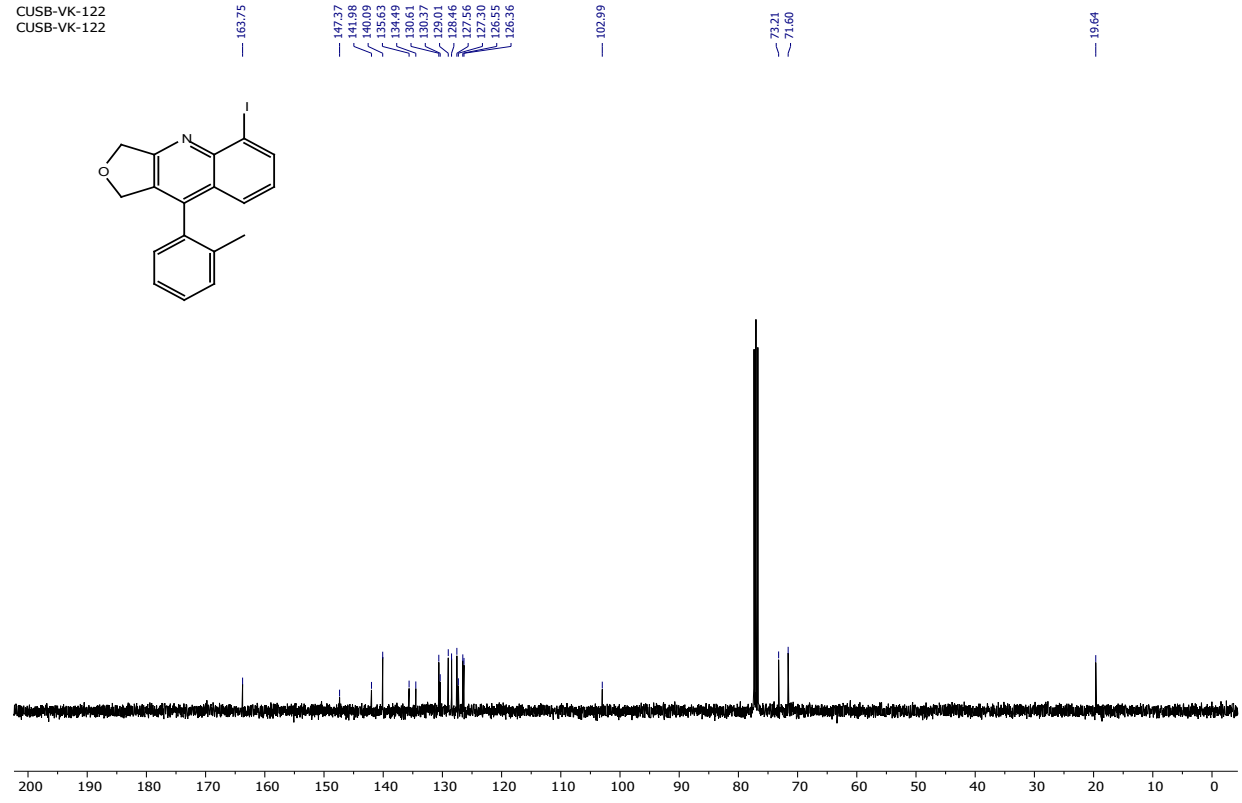
Compound 3h, ^{1}H NMR, $CDCl_3$, 400 MHz

CUSB-VK-122.10.1.1r
CUSB-VK-122



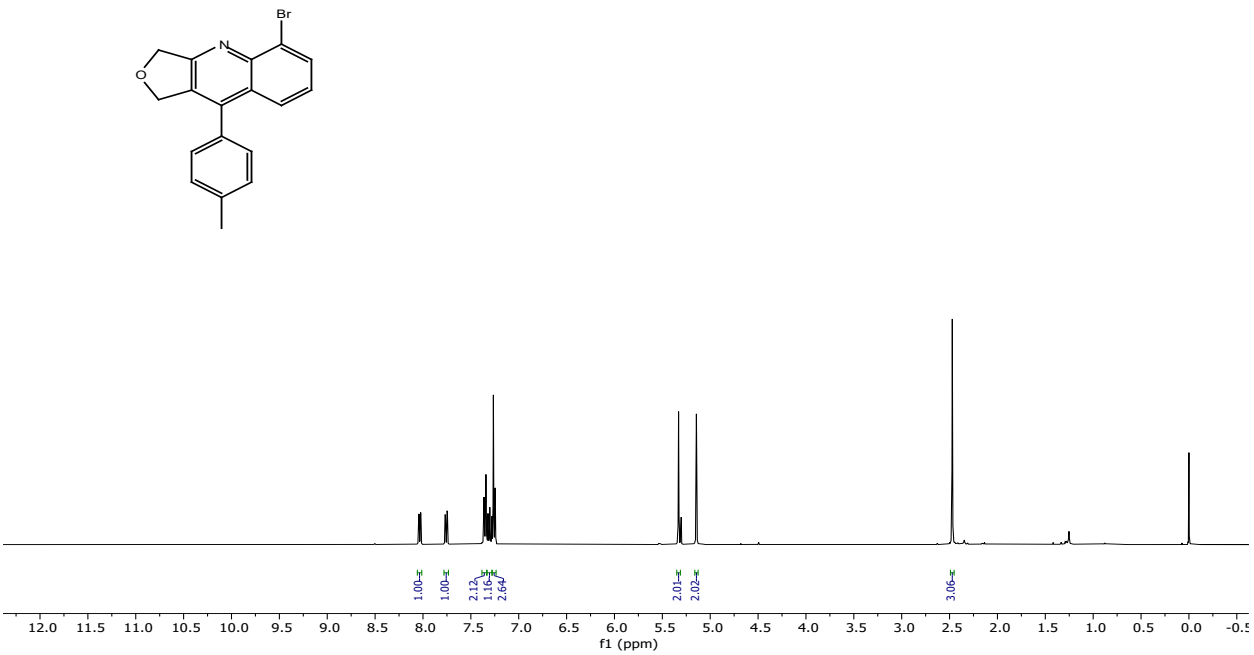
Compound 3h, ^{13}C NMR, $CDCl_3$, 101 MHz

CUSB-VK-122
CUSB-VK-122



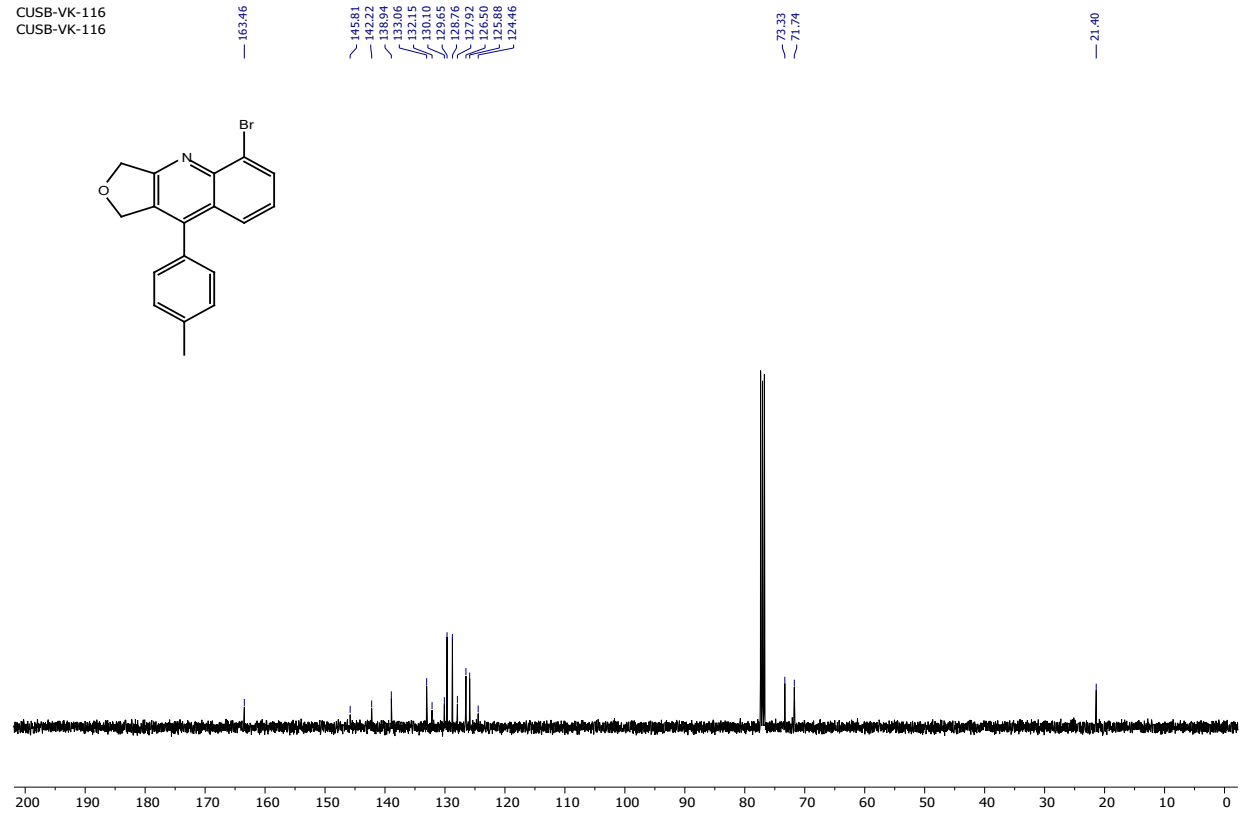
Compound 3i, ^{1}H NMR, $CDCl_3$, 400 MHz

CUSB-VK-116.10.1.1r
CUSB-VK-116

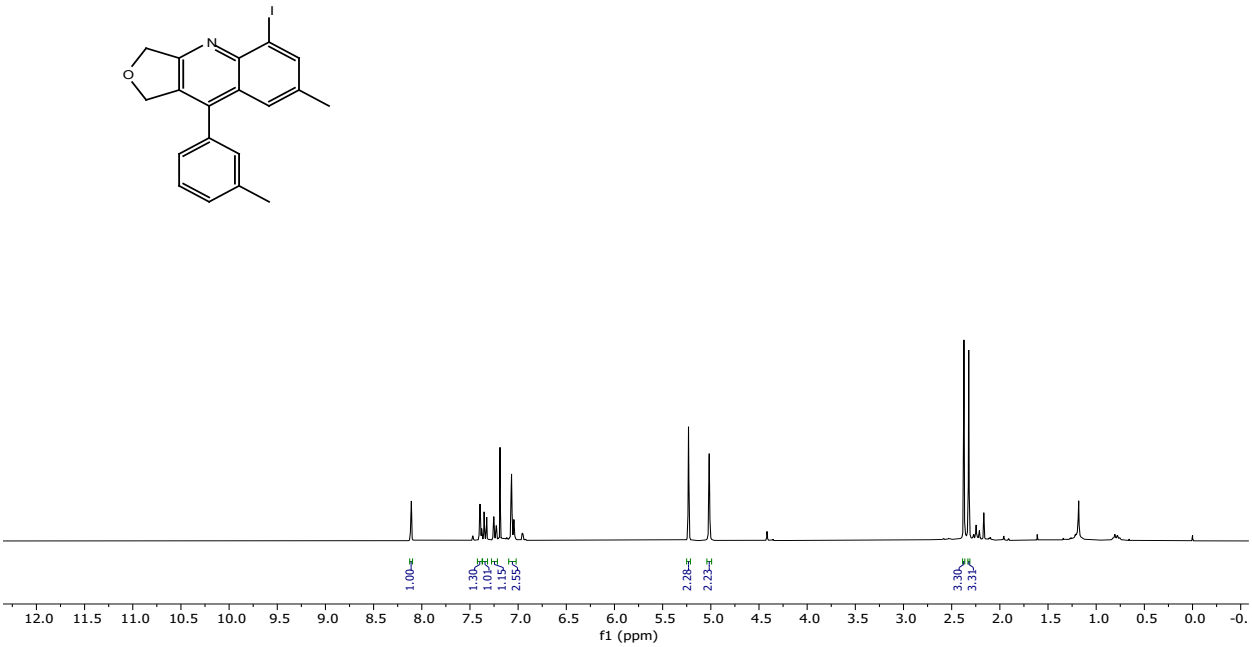


Compound 3i, ^{13}C NMR, $CDCl_3$, 101 MHz

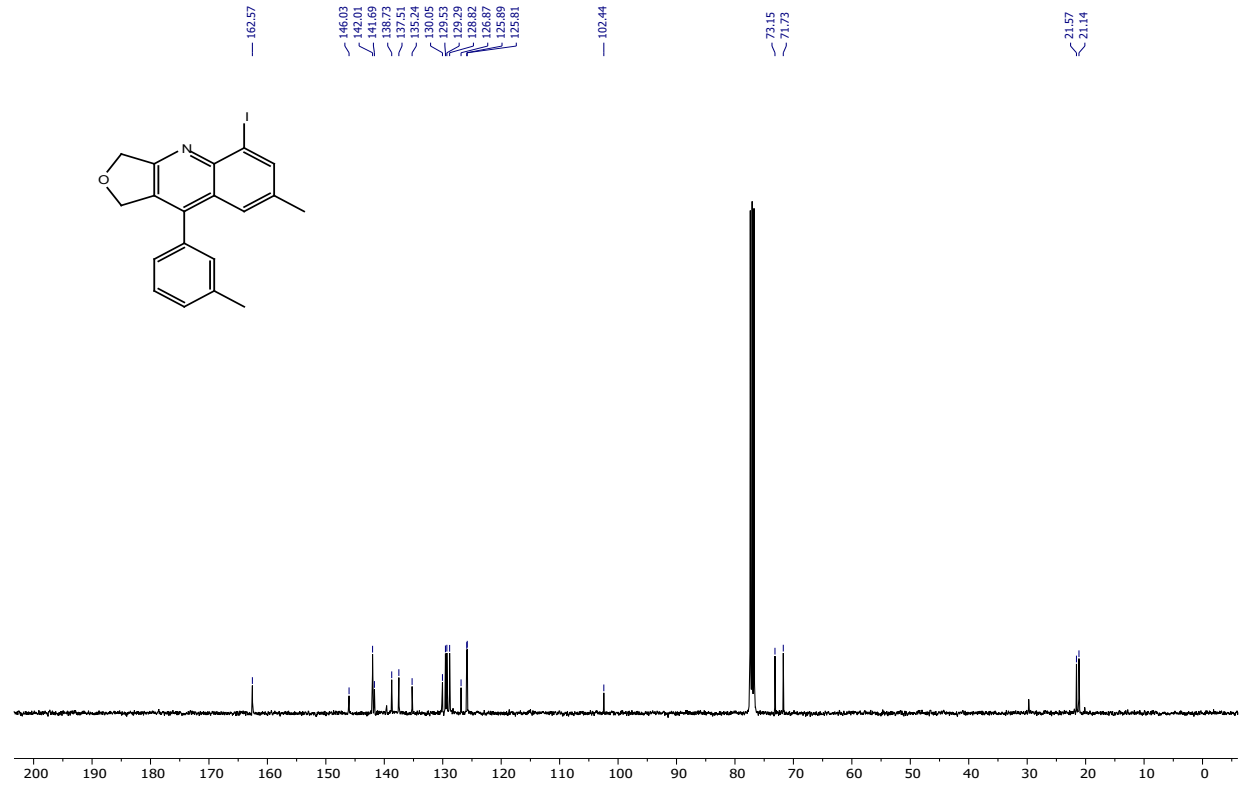
CUSB-VK-116
CUSB-VK-116



Compound 3j, ^{1}H NMR, $CDCl_3$, 400 MHz

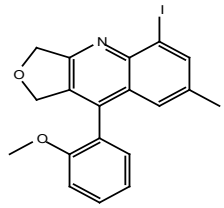


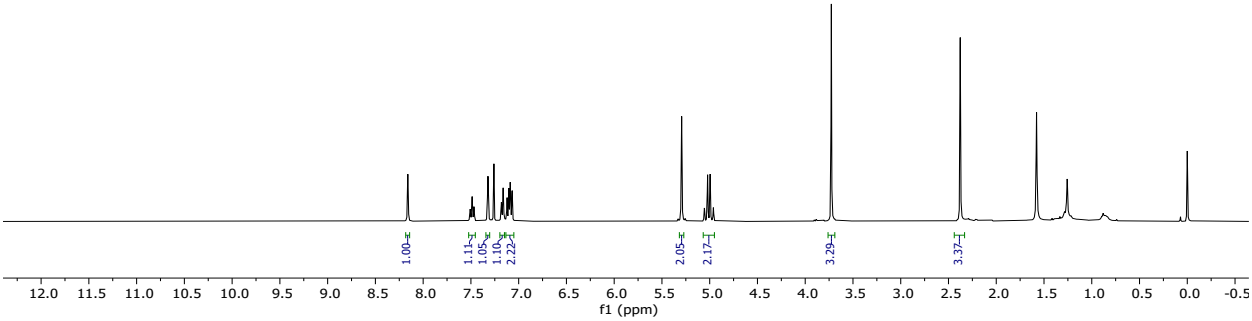
Compound 3j, ^{13}C NMR, $CDCl_3$, 101 MHz



Compound 3k, ^{1}H NMR, $CDCl_3$, 400 MHz

EXT40524.7.1.1r
Signature SIF VIT VELLORE
CUSBVK198-LS

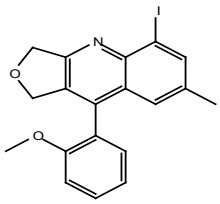




Compound 3k, ^{13}C NMR, $CDCl_3$, 101 MHz

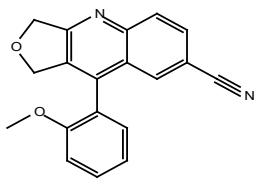
EXT40524
Signature SIF VIT VELLORE
CUSBVK198-US

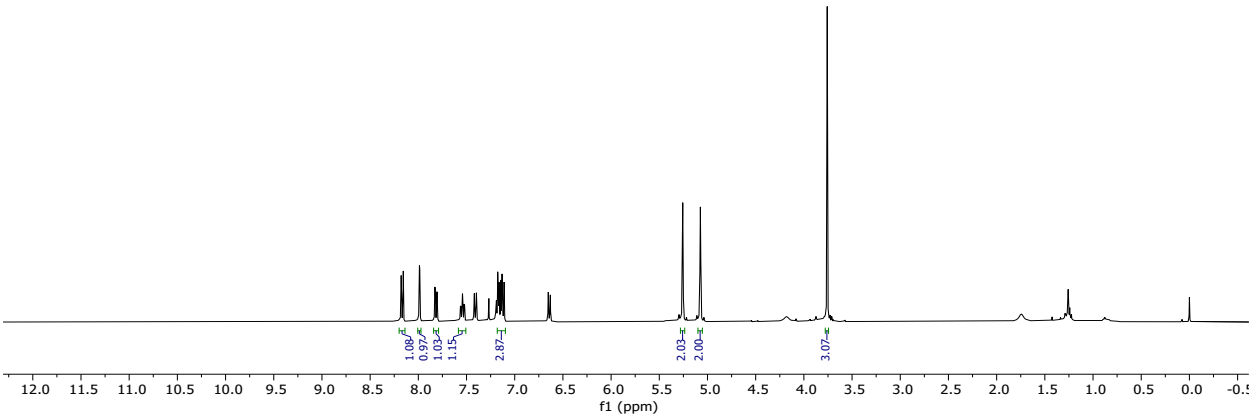
162.44 156.53 146.14 141.66 138.10 137.16 130.98 130.67 130.39 127.22 125.78 123.65 120.81 111.40 102.74 73.15 71.95 55.50 21.07



Compound 3l, ^{1}H NMR, $CDCl_3$, 400 MHz

EXT40524.33.1.1r
Signature SIF VIT VELLORE
CUSBVK199-US

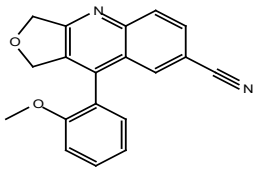


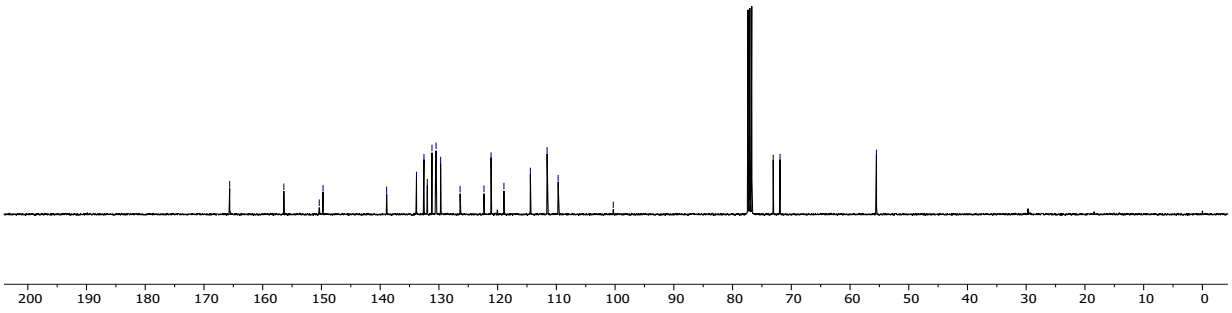


Compound 3l, ^{13}C NMR, $CDCl_3$, 101MHz

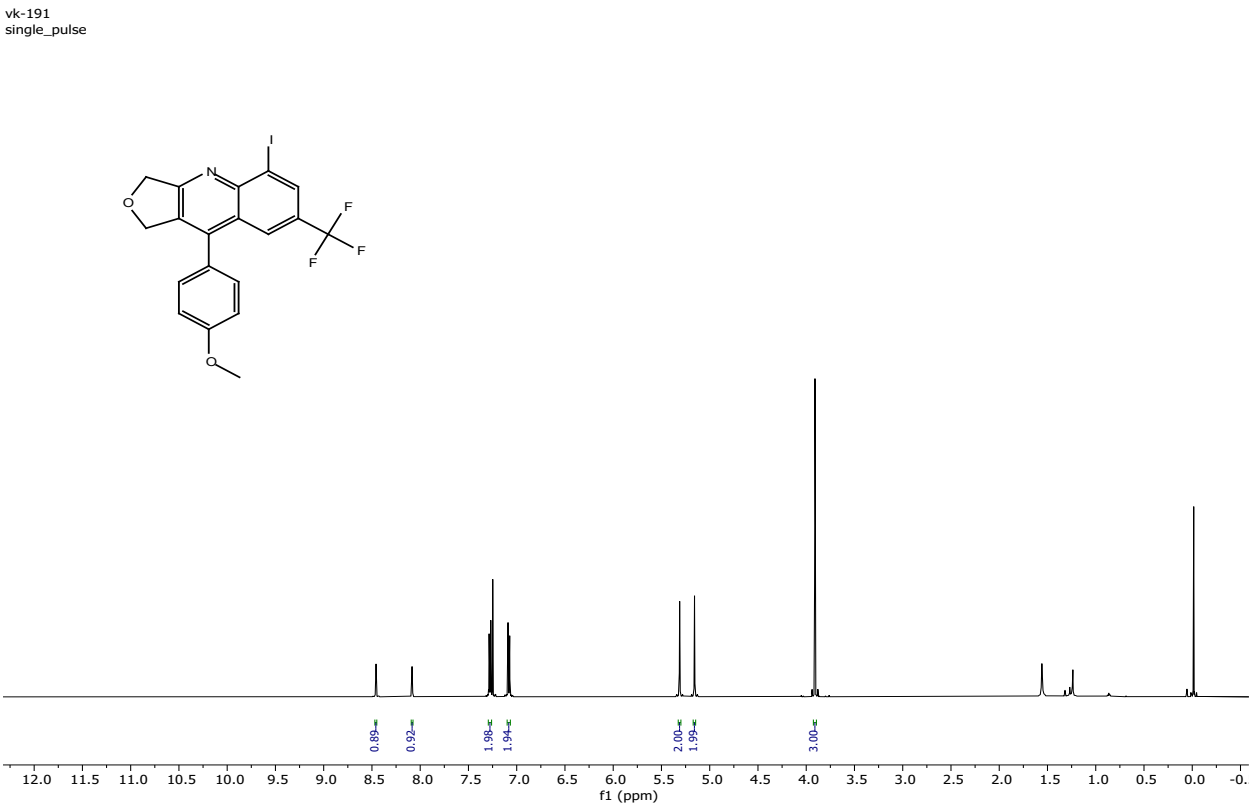
EXT40524
Signature SIF VIT VELLORE
CUSBVK199-US

165.62
156.40
150.37
149.73
138.90
133.82
132.54
131.97
131.18
130.56
130.48
129.70
126.39
122.33
121.12
118.93
114.43
111.58
109.70
100.31
73.08
71.91
55.50

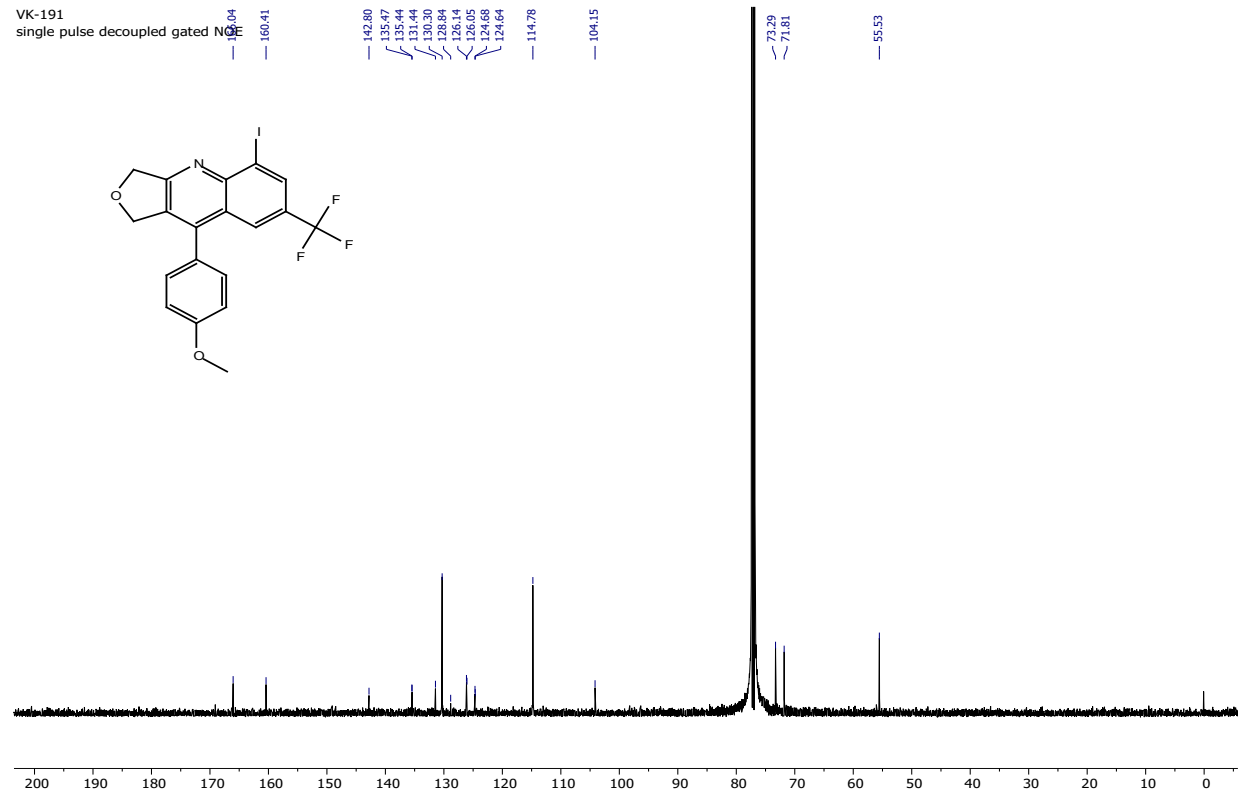




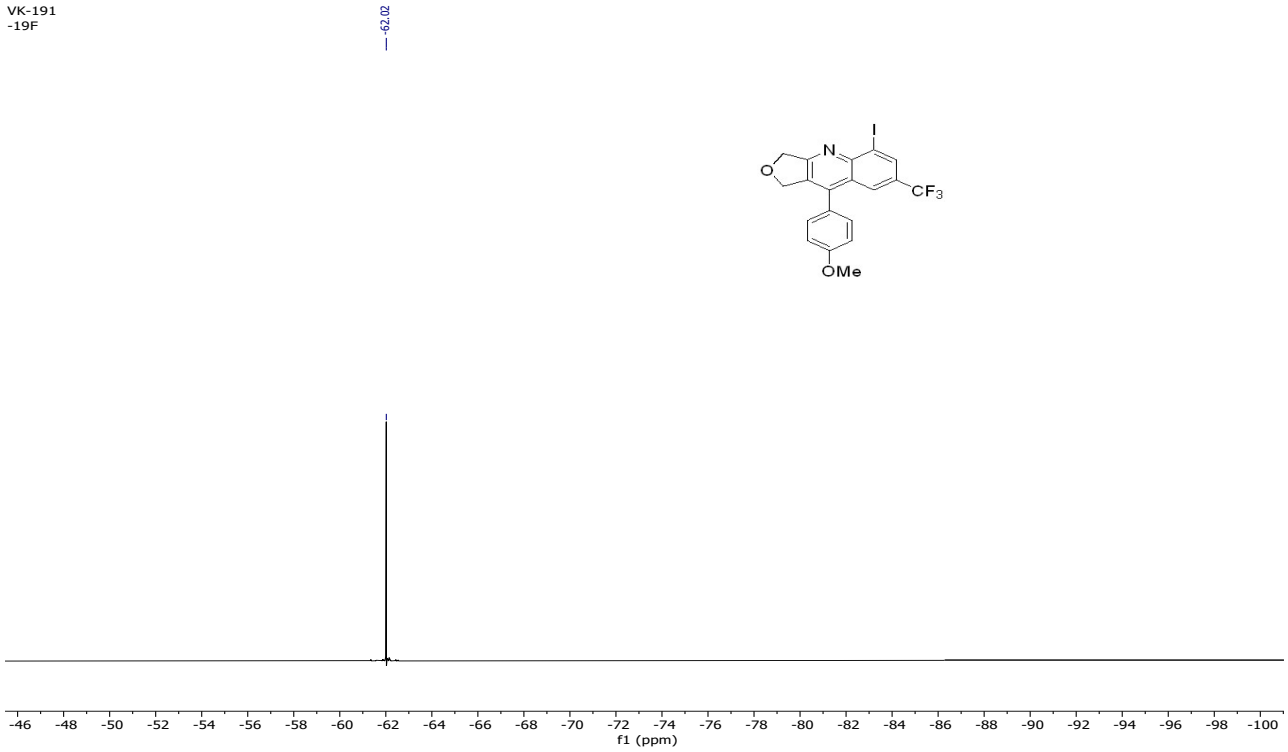
Compound 3m, ^{1}H NMR, $CDCl_3$, 500 MHz



Compound 3m, ^{13}C NMR, $CDCl_3$, 126 MHz

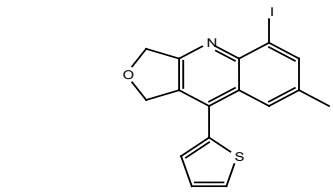


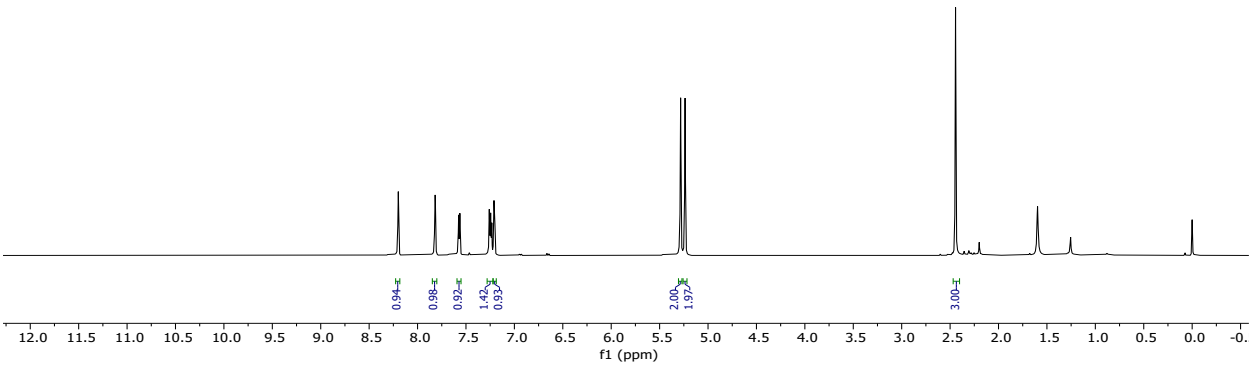
Compound 3m, ^{19}F NMR, $CDCl_3$, 471 MHz



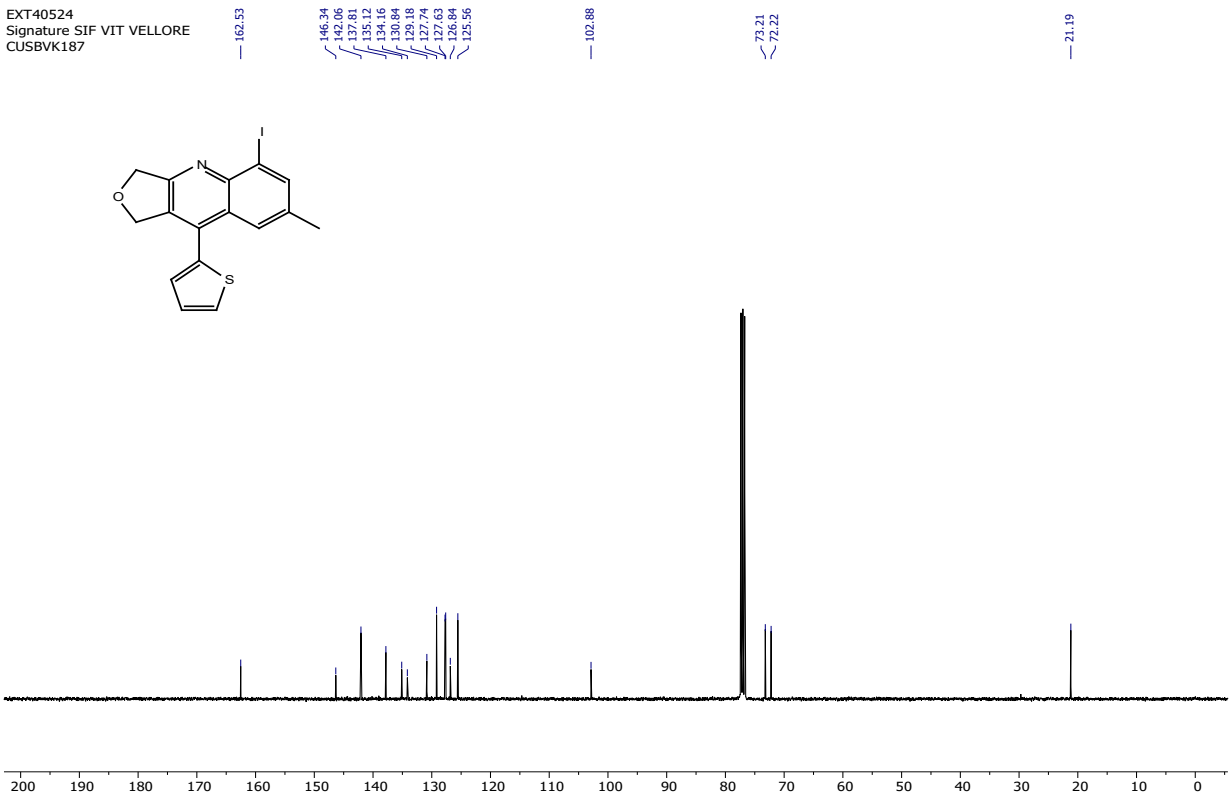
Compound 3n, ^{1}H NMR, $CDCl_3$, 400 MHz

EXT40524.5.1.1r
Signature SIF VIT VELLORE
CUSBVK187

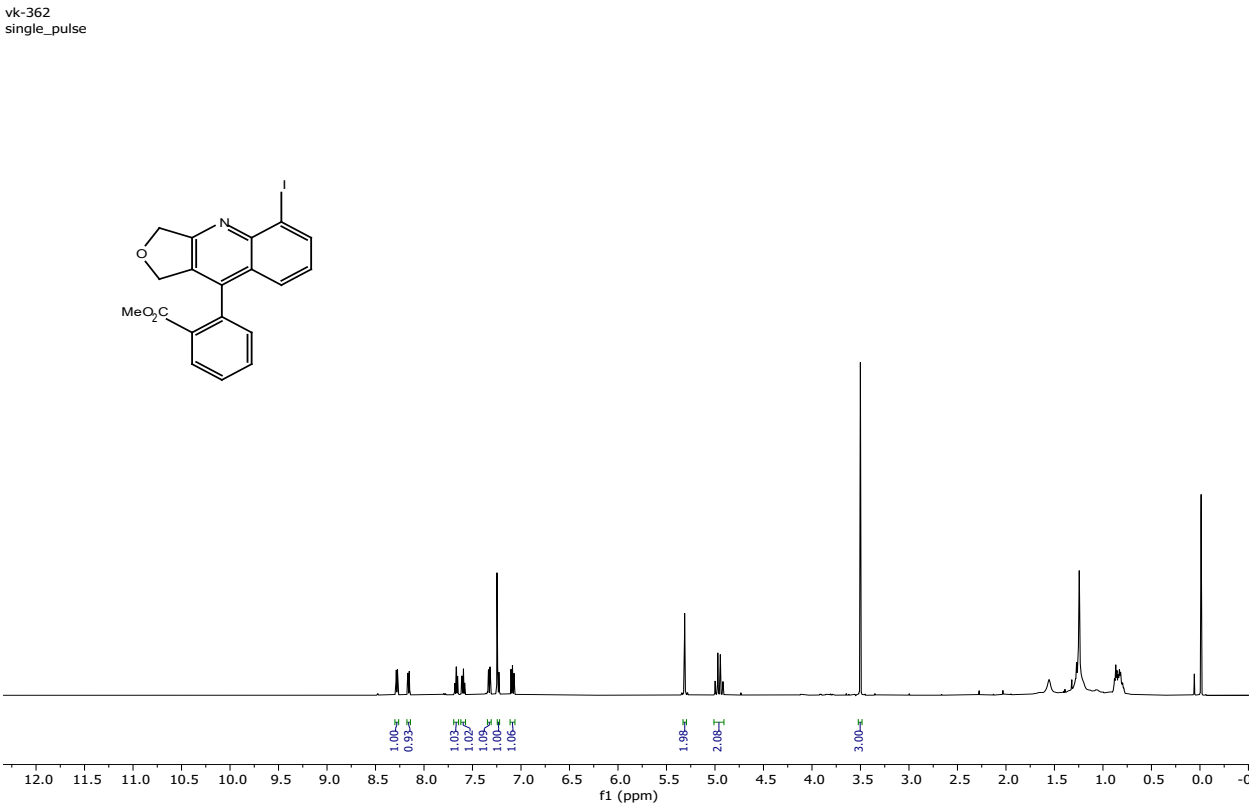




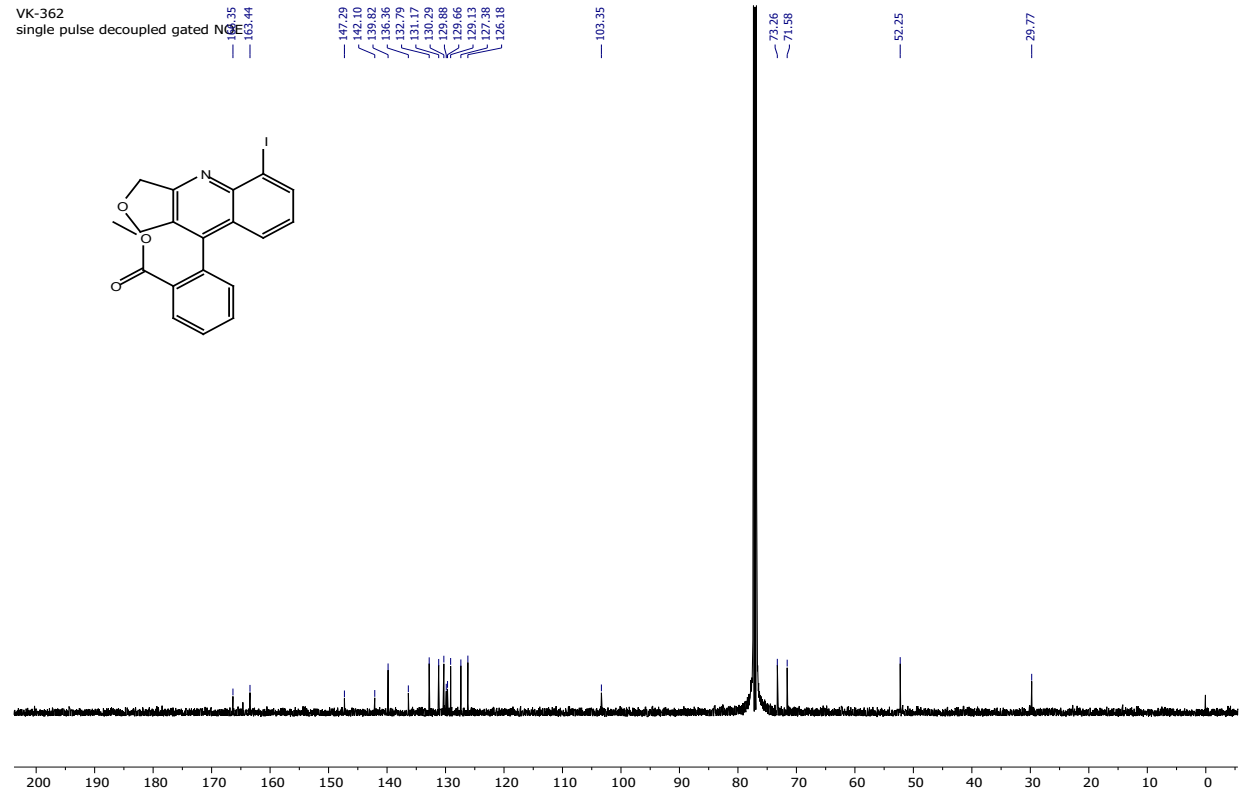
Compound 3n, ^{13}C NMR, $CDCl_3$, 101MHz



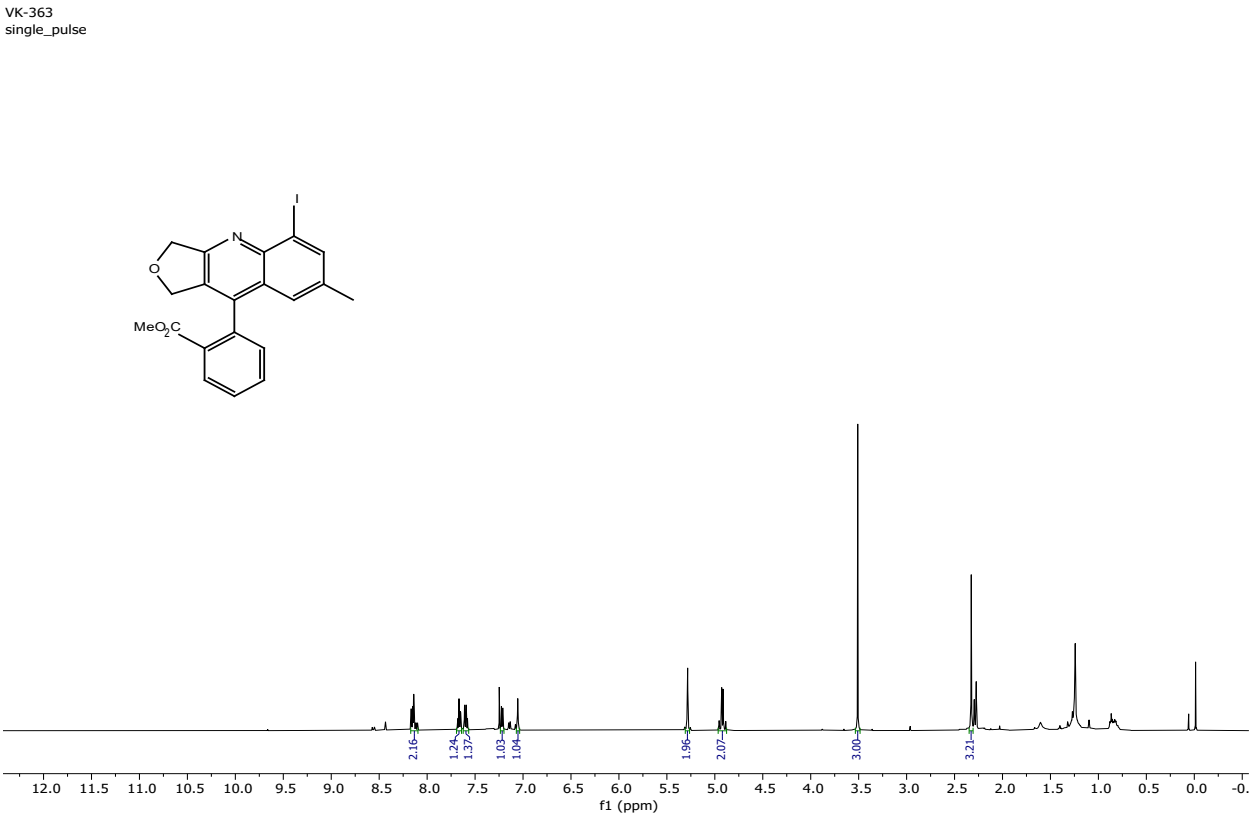
Compound 3o, ^{1}H NMR, $CDCl_3$, 500 MHz



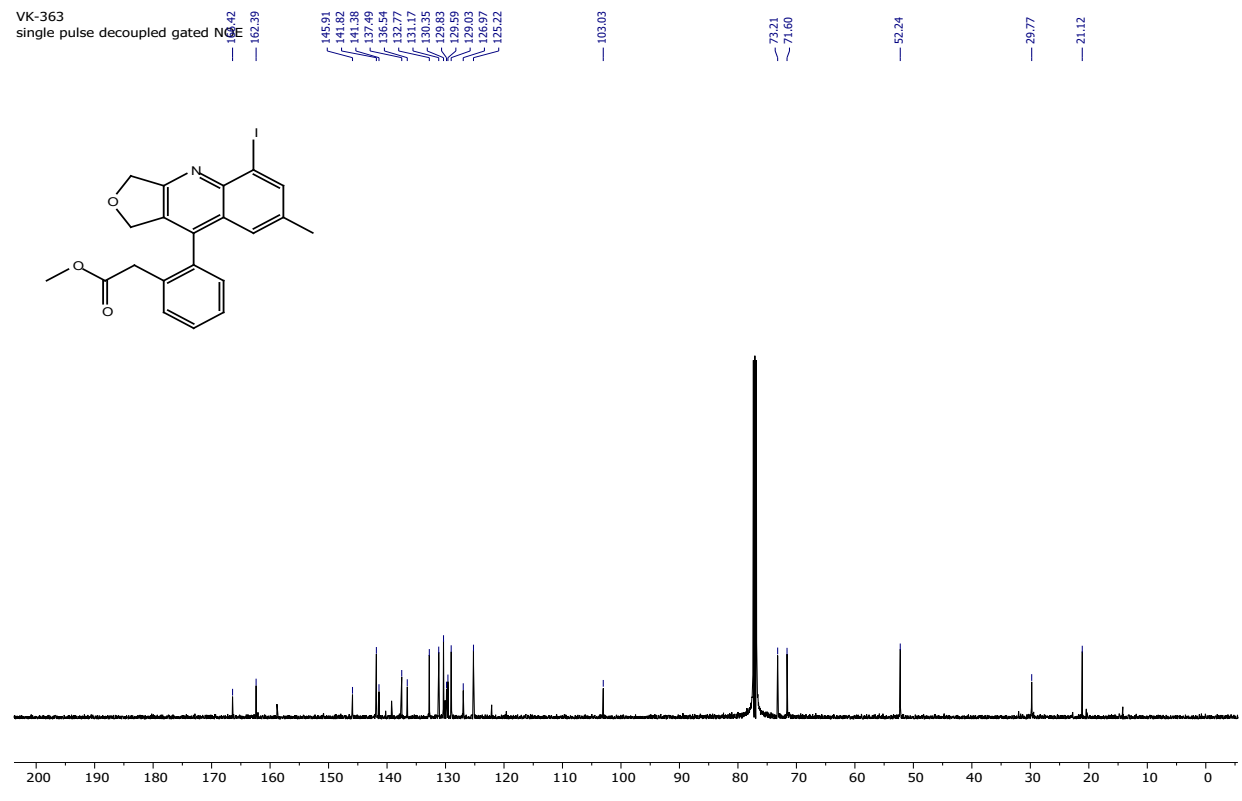
Compound 3o, ^{13}C NMR, $CDCl_3$, 126 MHz



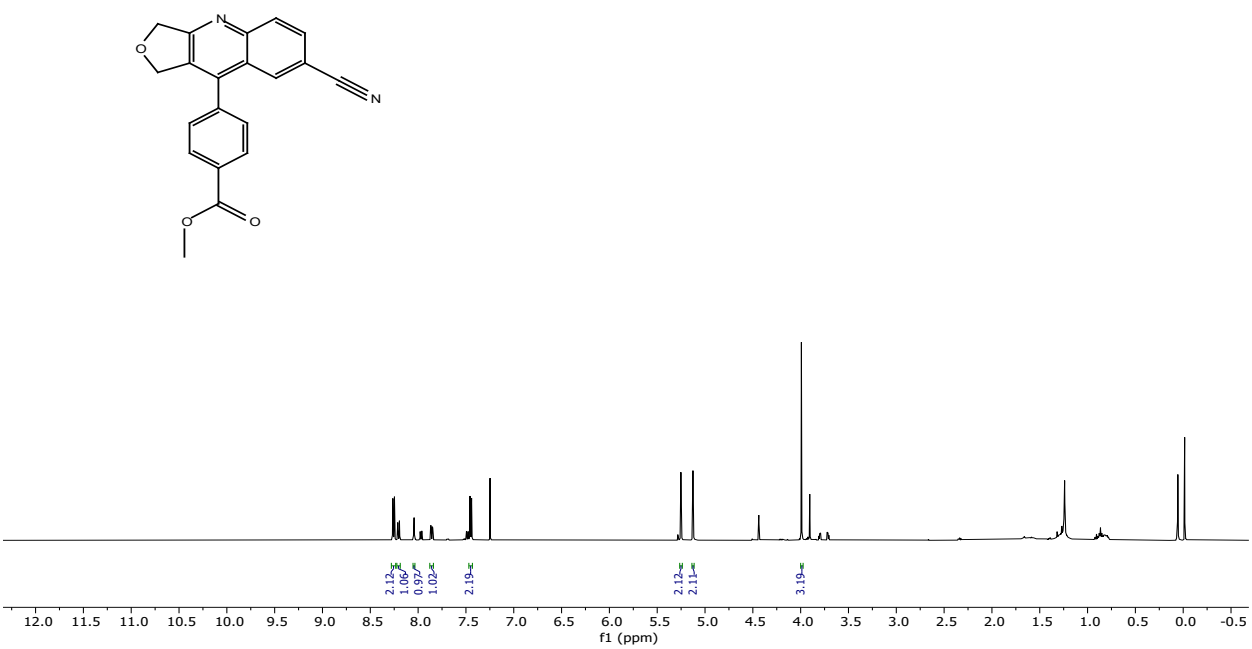
Compound 3p, ^{1}H NMR, $CDCl_3$, 500 MHz



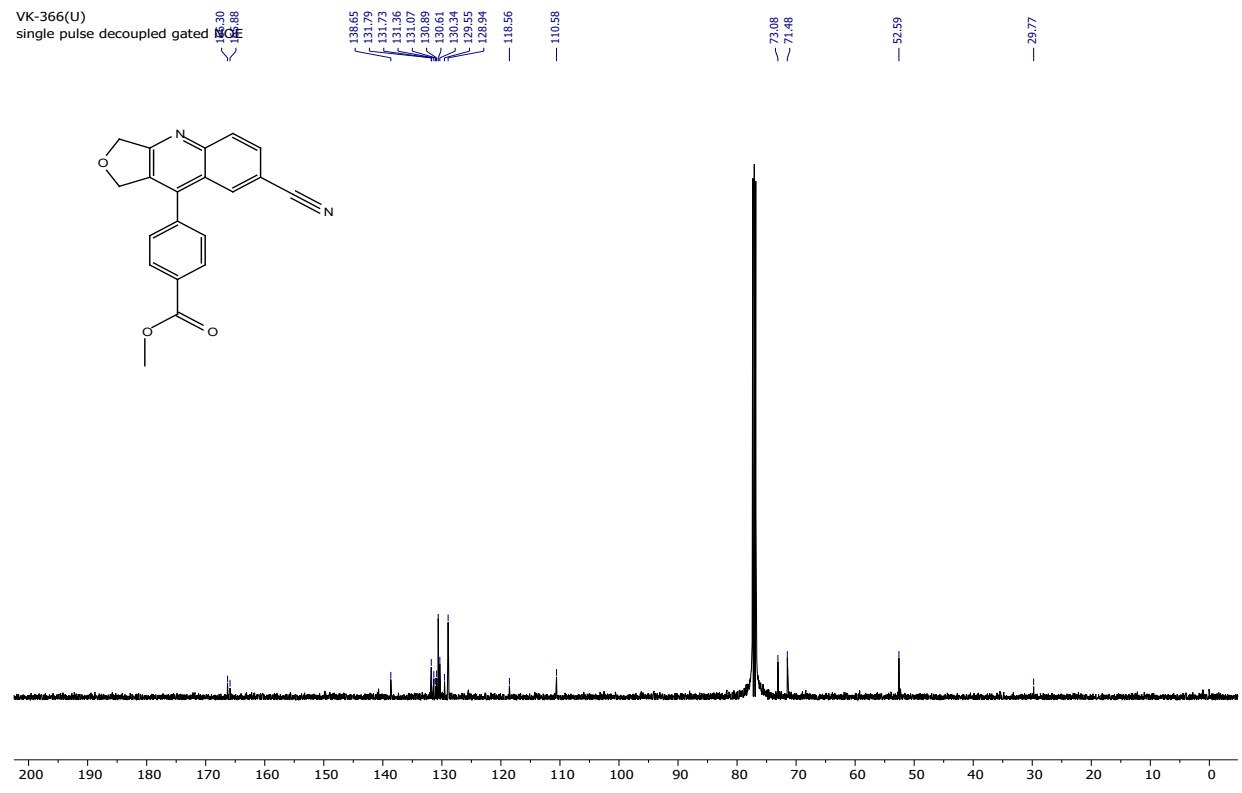
Compound 3p, ^{13}C NMR, $CDCl_3$, 126 MHz



Compound 3q, ^{1}H NMR, $CDCl_3$, 500 MHz

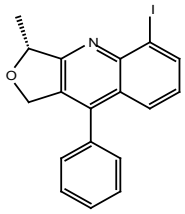


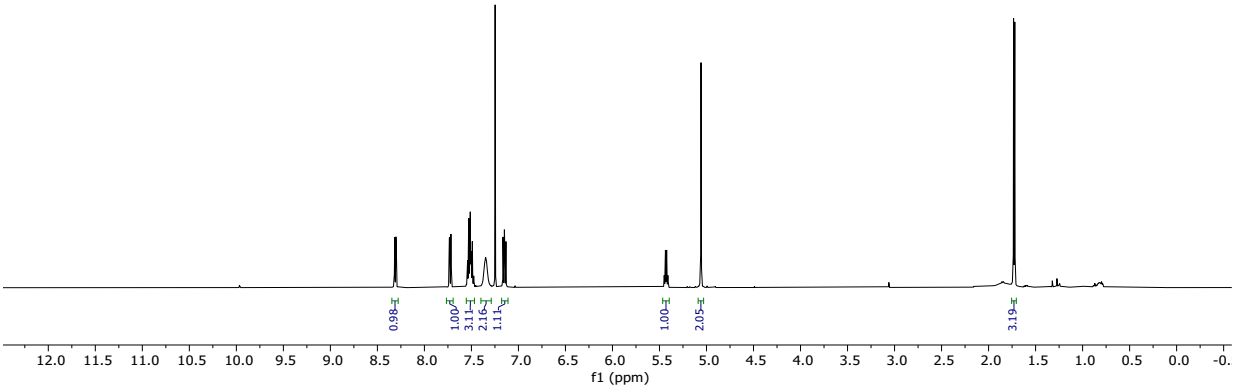
Compound 3q, ^{13}C NMR, $CDCl_3$, 126 MHz



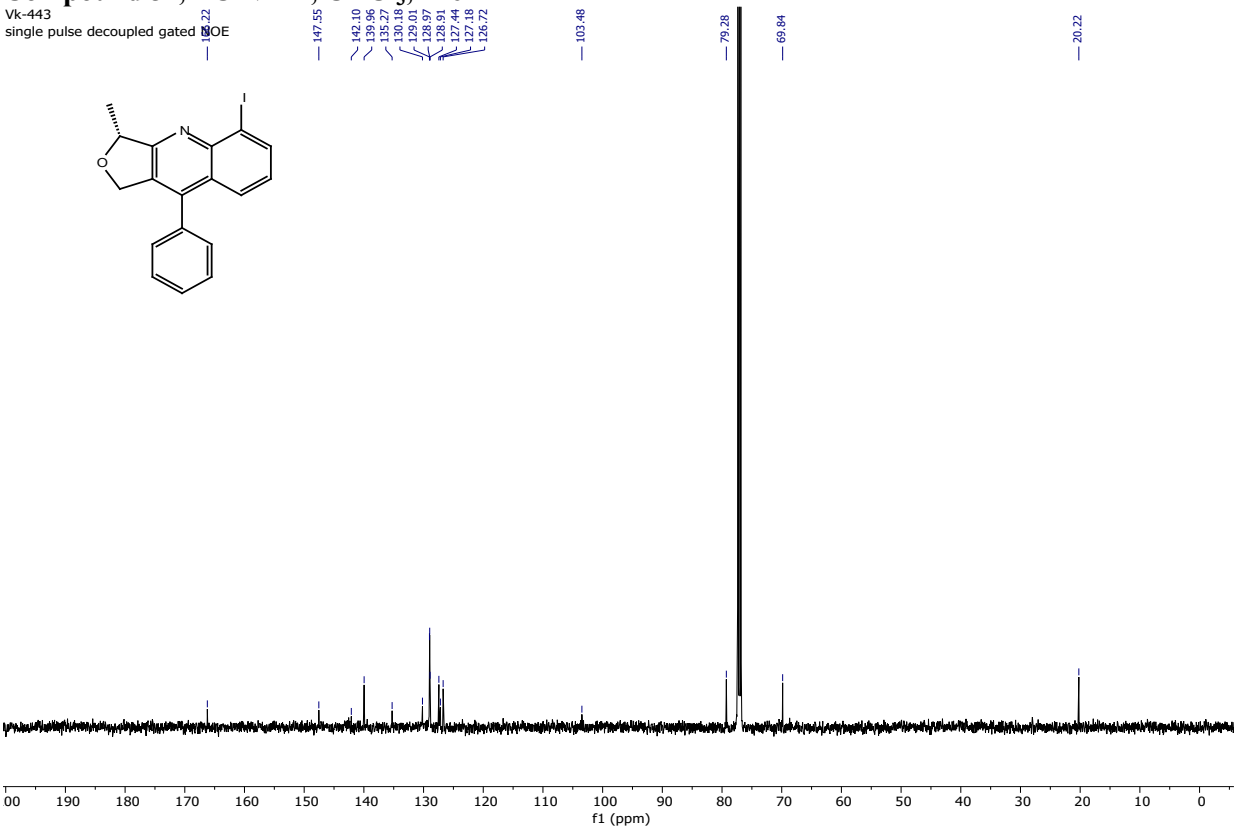
Compound 3r, ^{1}H NMR, $CDCl_3$, 500 MHz

Vk-443
single_pulse



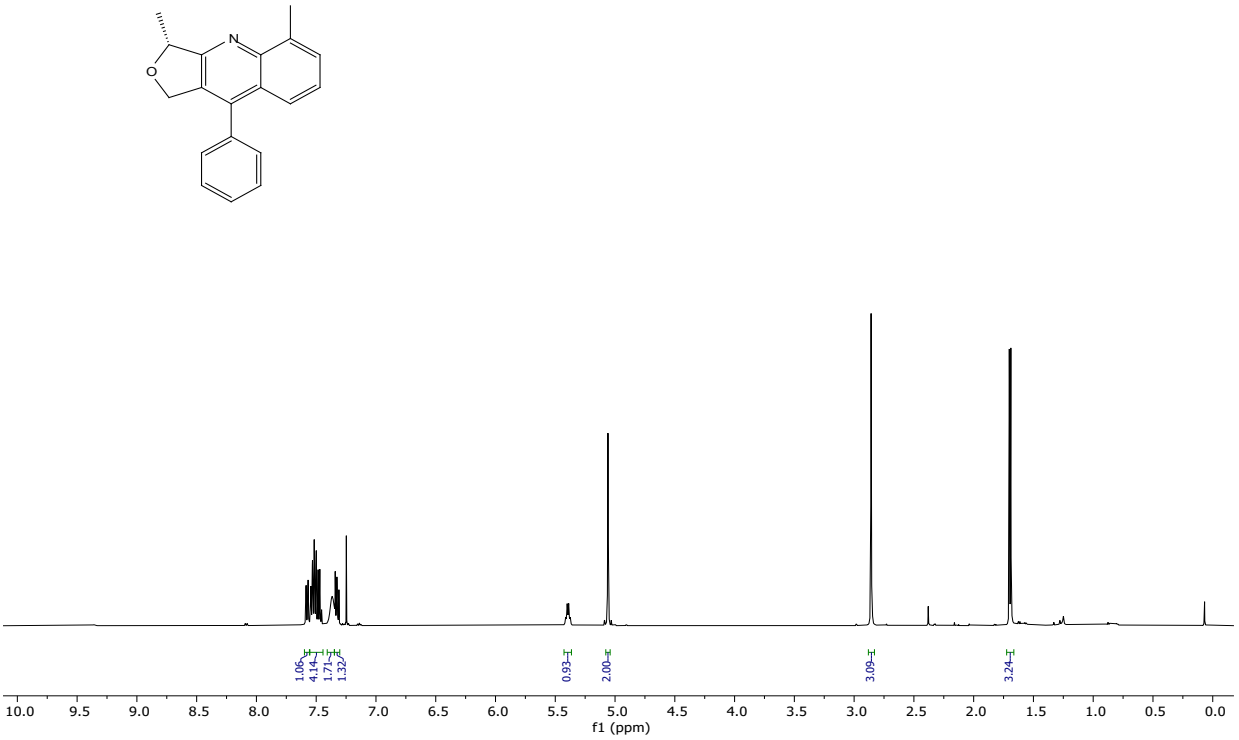


Compound 3r, ^{13}C NMR, $CDCl_3$, 126 MHz



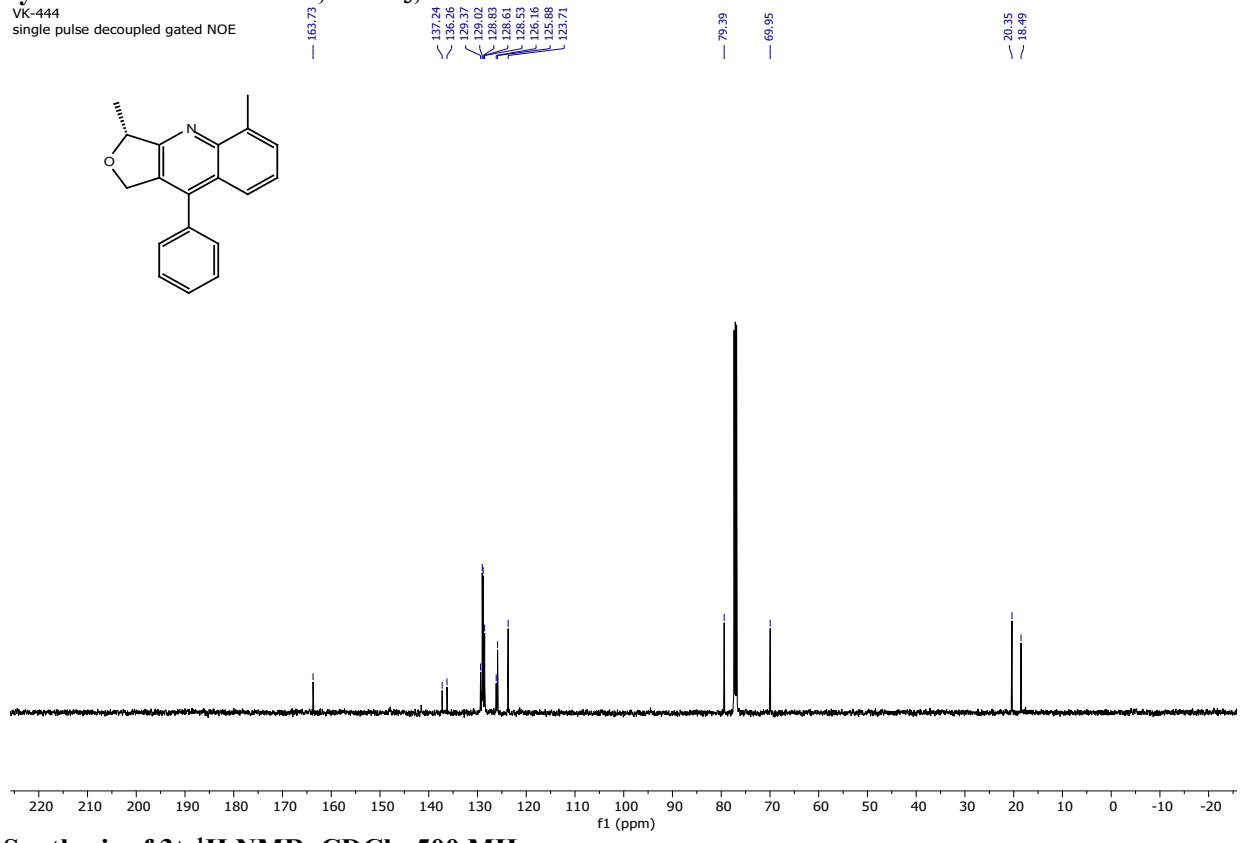
Compound 3s, ^{1}H NMR, $CDCl_3$, 500 MHz

VK-444
single_pulse



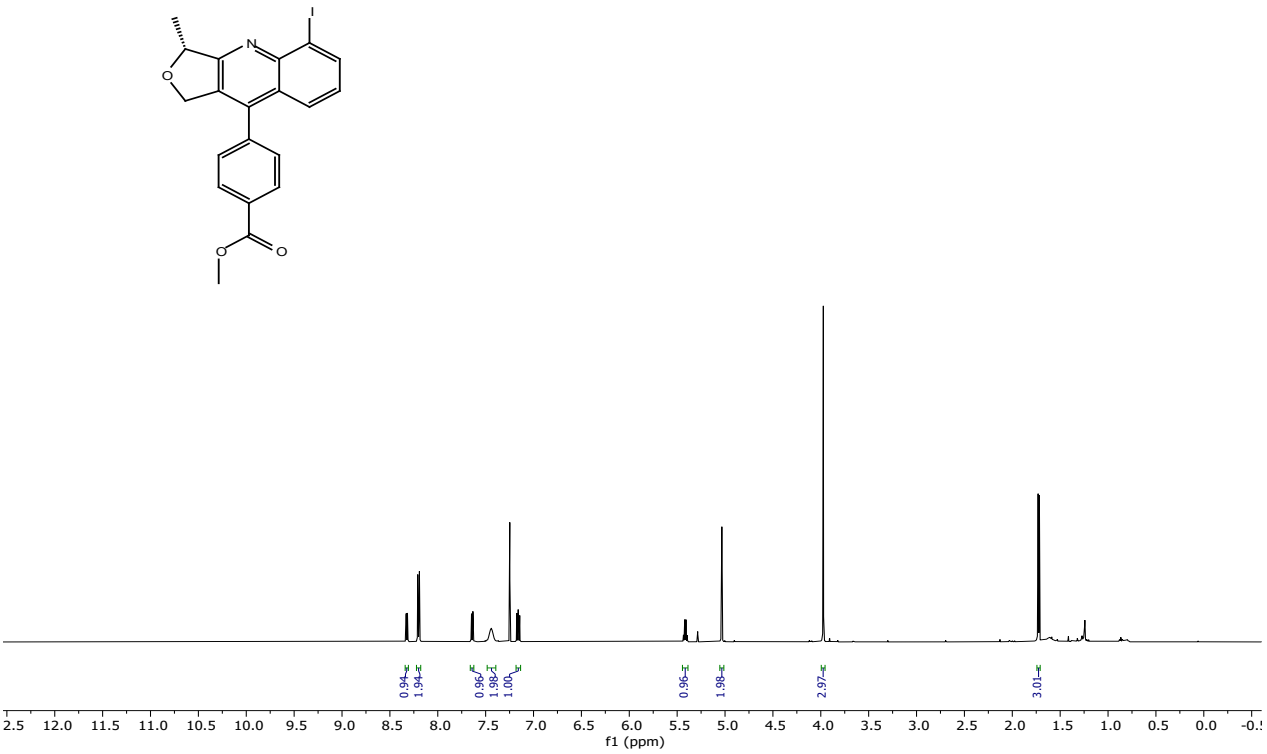
Synthesis of 3s. ^{13}C NMR, $CDCl_3$, 126 MHz

VK-444
single pulse decoupled gated NOE



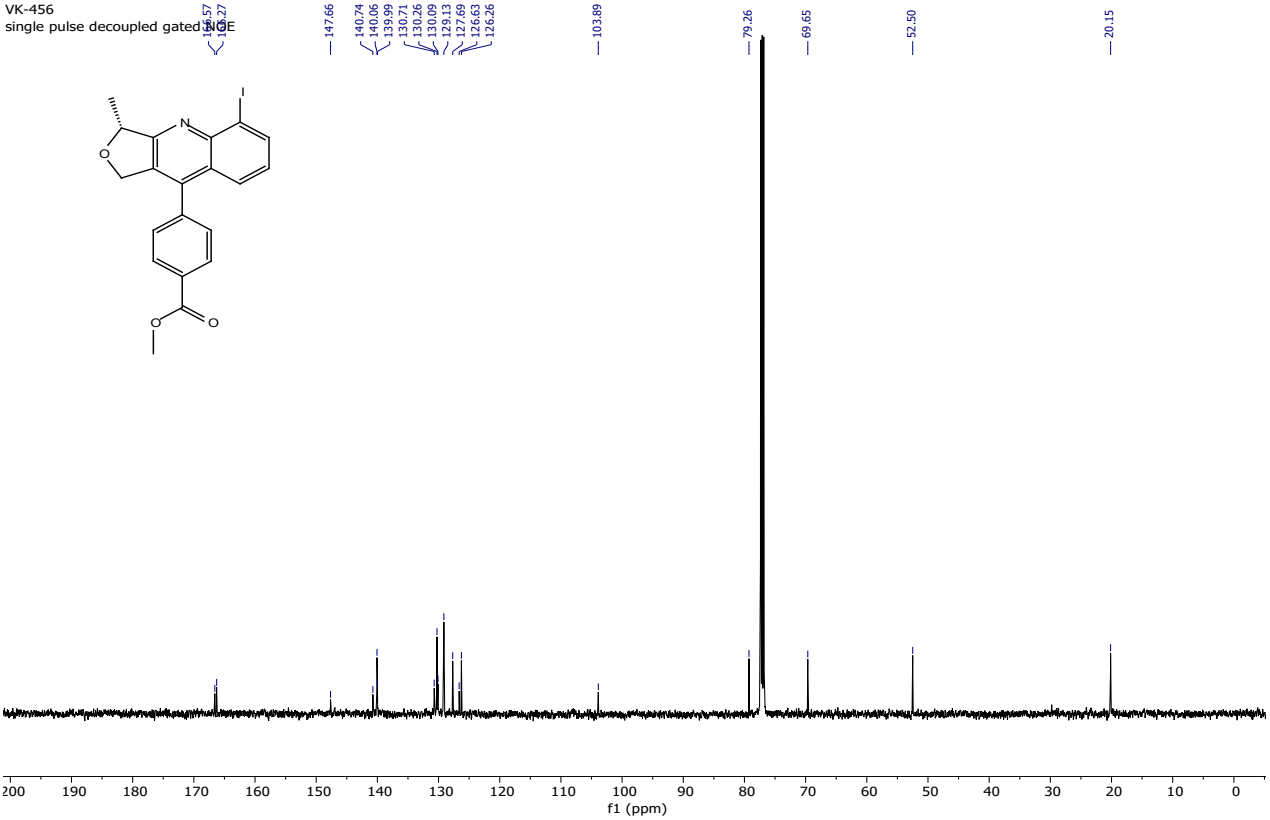
Synthesis of 3t, ^{1}H NMR, $CDCl_3$, 500 MHz

VK-456
single_pulse



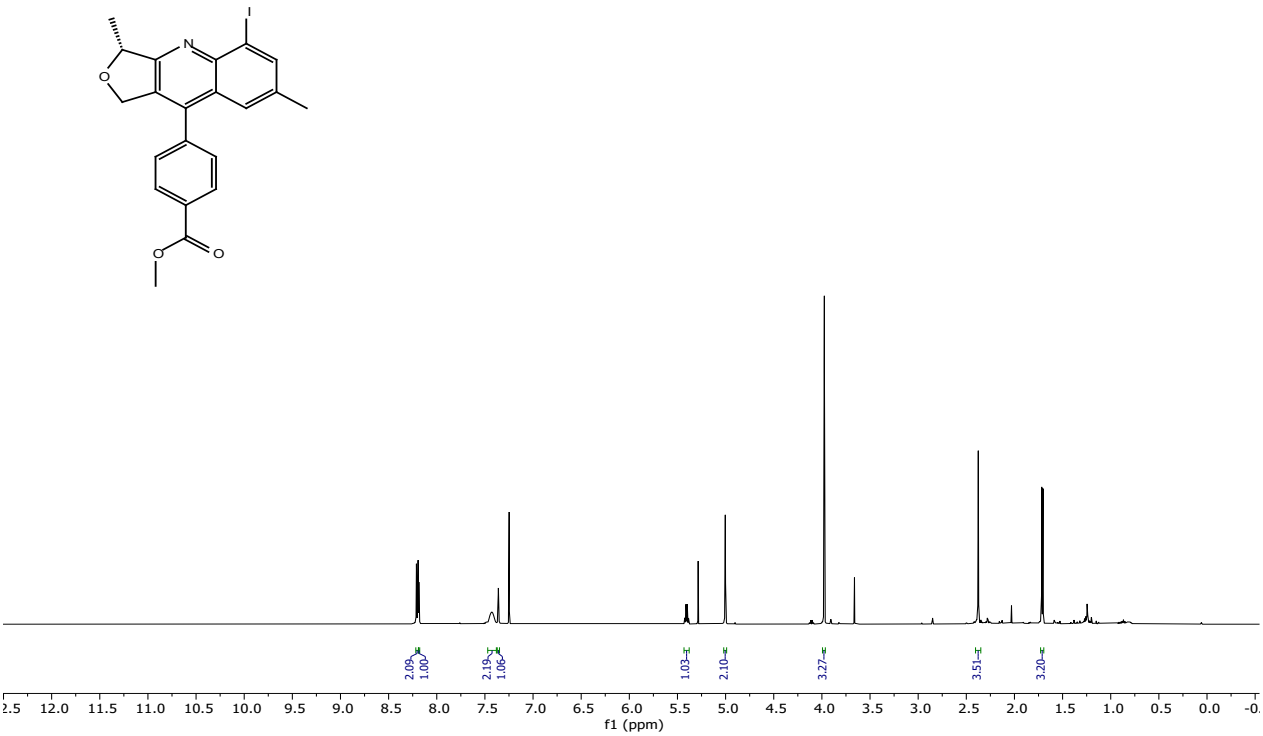
Compound 3t, ^{13}C NMR, $CDCl_3$, 126 MHz

VK-456
single pulse decoupled gated NOE

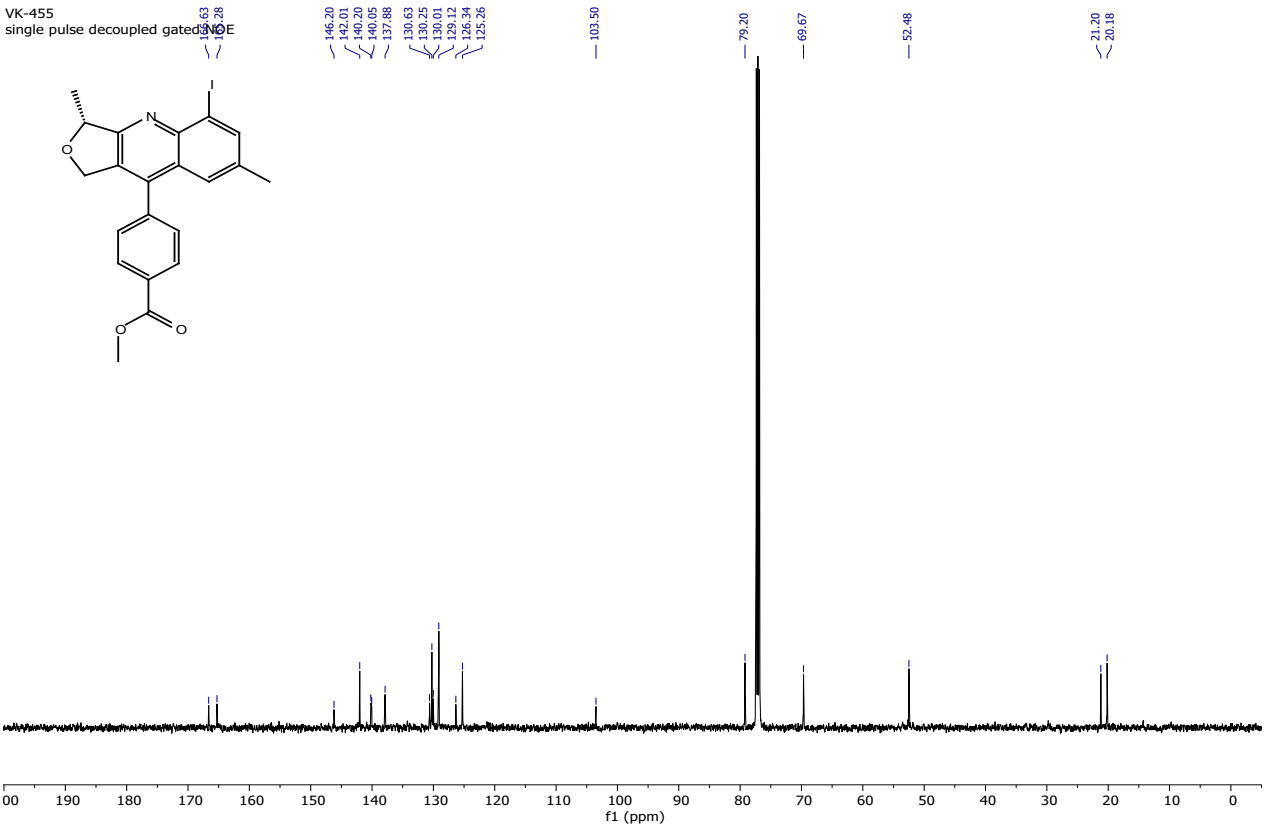


Compound 3u, ^{1}H NMR, $CDCl_3$, 500 MHz

VK-455
single_pulse

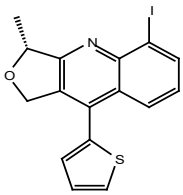


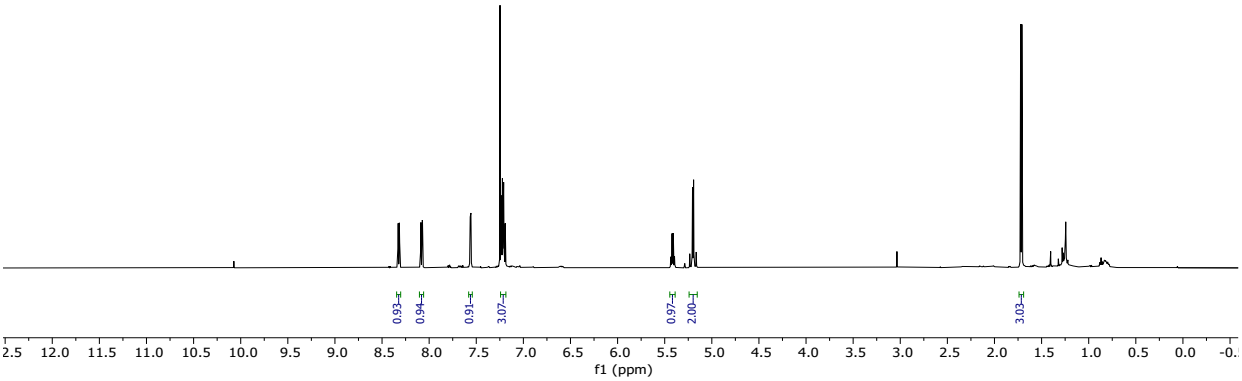
Compound 3u, ^{13}C NMR, $CDCl_3$, 126MHz



Compound 3v, ^{1}H NMR, $CDCl_3$, 500 MHz

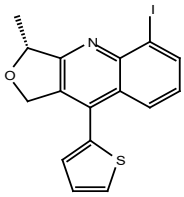
VK-454
single_pulse





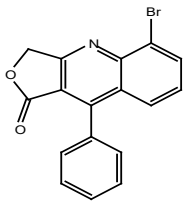
Compound 3v, ^{13}C NMR, $CDCl_3$, 126 MHz

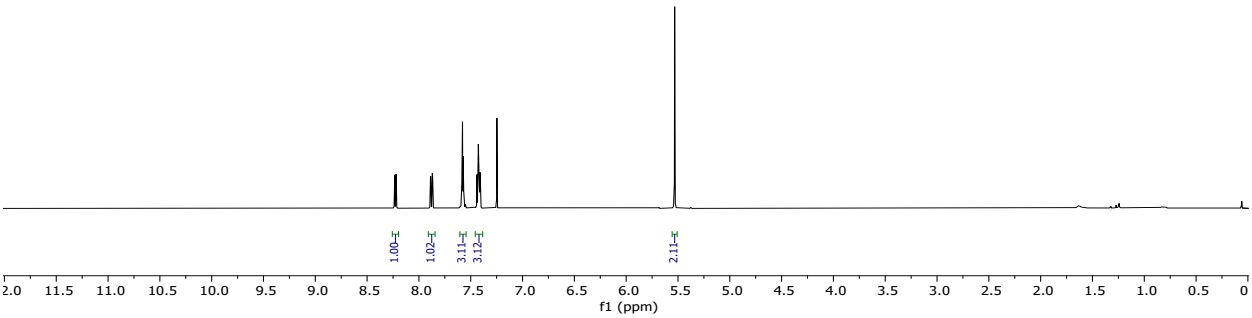
VK-454
single pulse decoupled gated NOE



Compound 4a, ^{1}H NMR, $CDCl_3$, 500 MHz

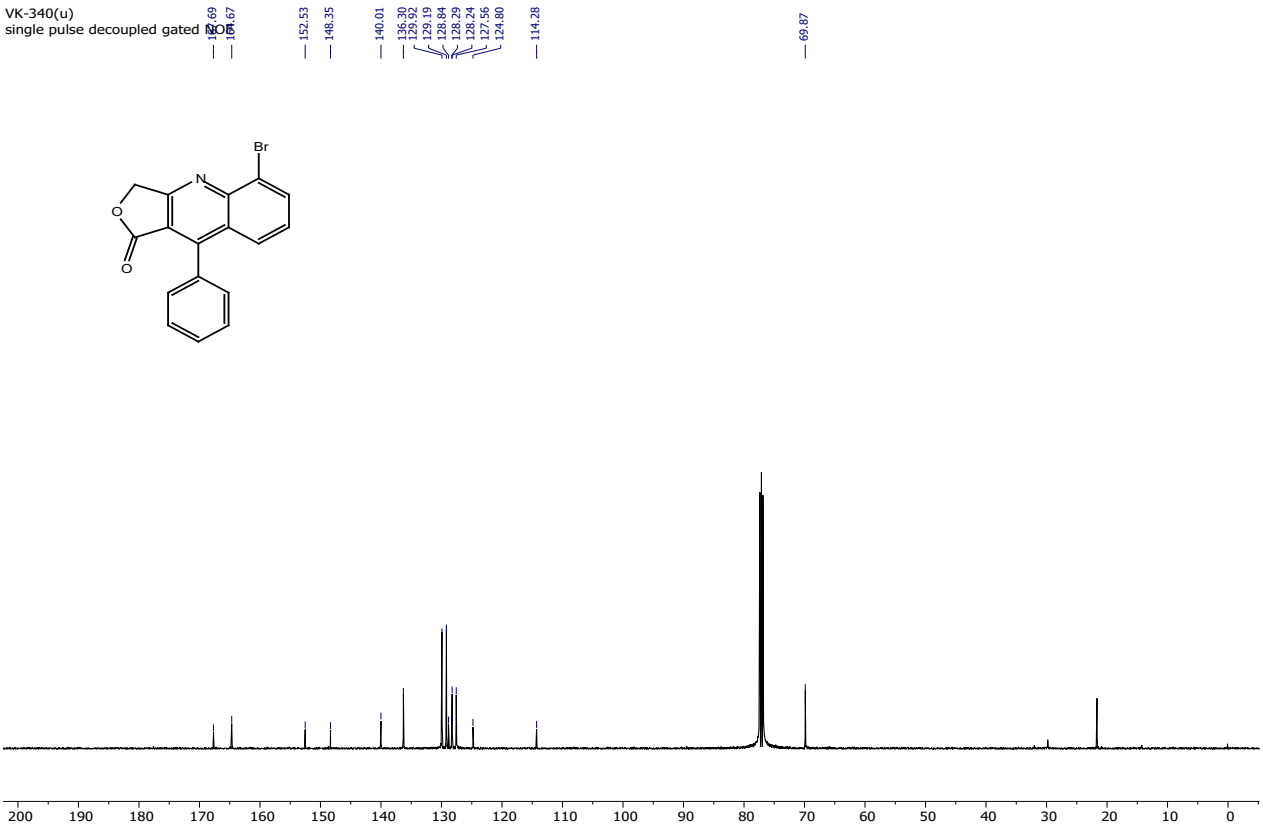
Vk-428
single_pulse





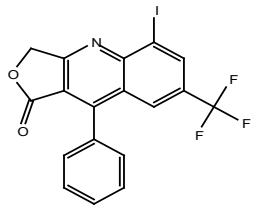
Compound 4a, ^{13}C NMR, $CDCl_3$, 126 MHz

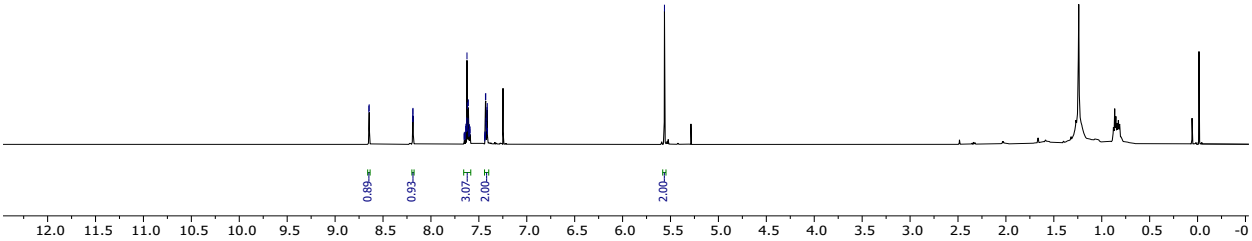
VK-340(u)
single pulse decoupled gated NOE



Compound 4b, ^{1}H NMR, $CDCl_3$, 500 MHz

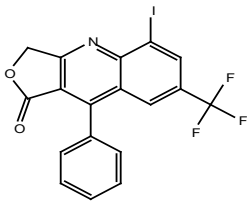
vk-340(D)
single_pulse

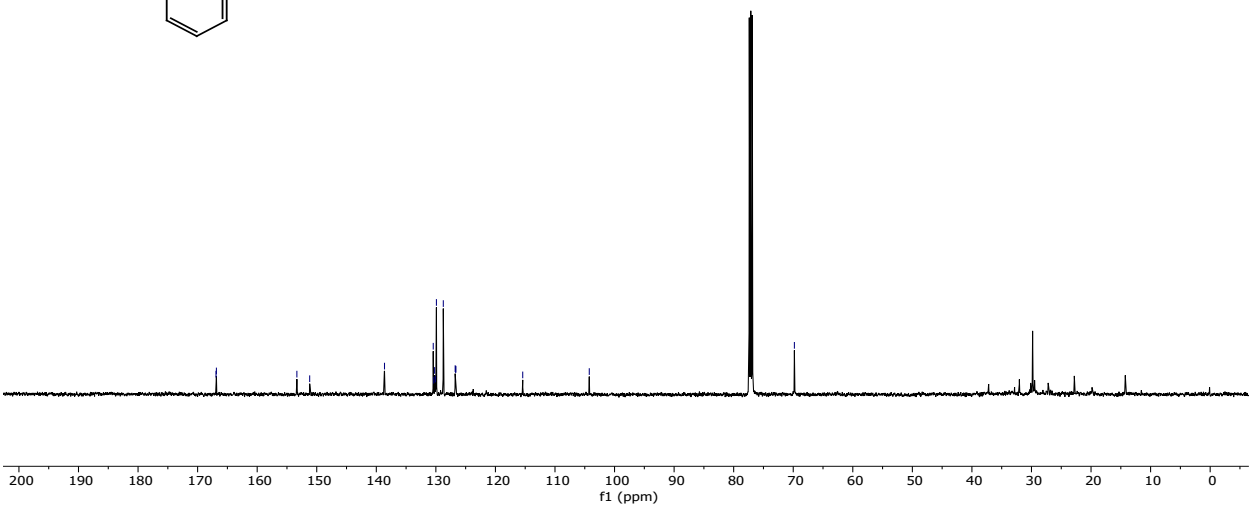




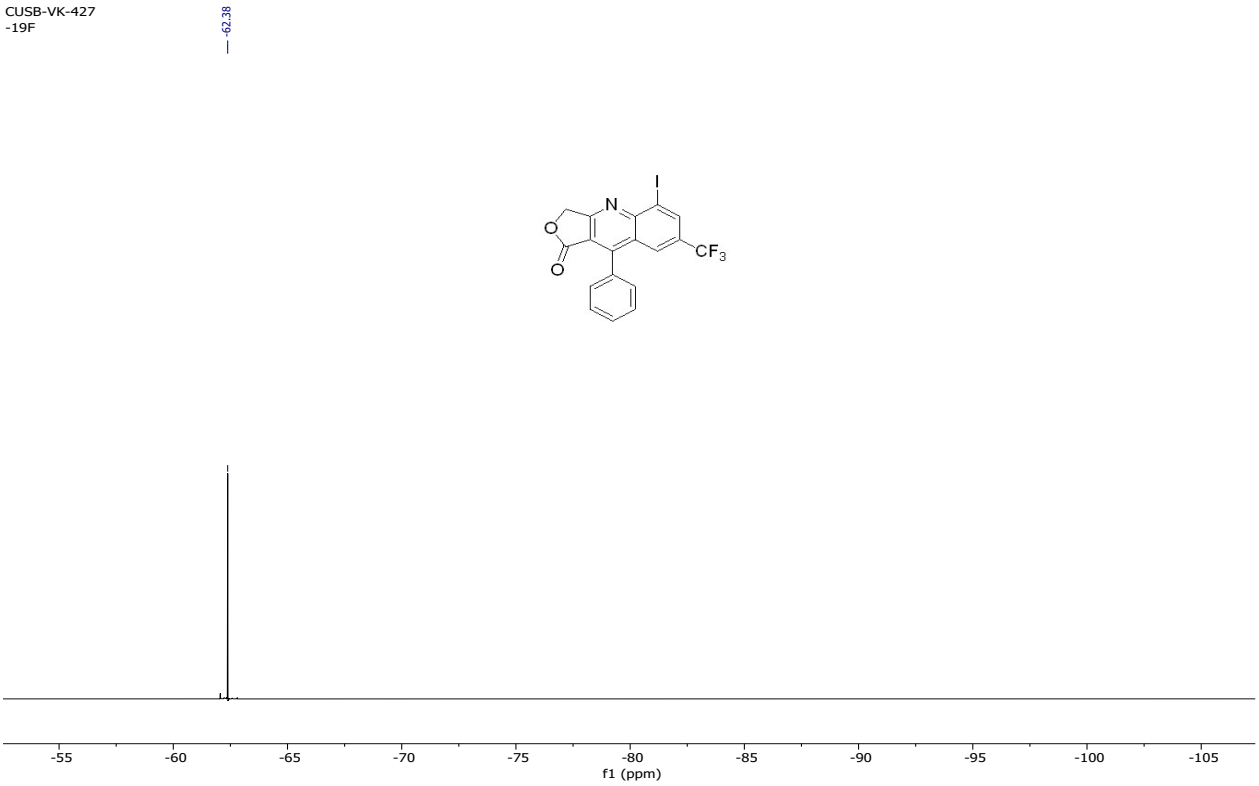
Compound 4b, ^{13}C NMR, $CDCl_3$, 126 MHz

VK-340(D)
single pulse decoupled gated NOE





Compound 4b, ^{19}F NMR, $CDCl_3$, 471 MHz



Sample Preparation and Crystal Structure Description

The pure compound **4a** as obtained from column chromatography was crystallized from a mixture solvent of hexanes and ethyl acetate (9:1). Compound **4a** crystallizes in the triclinic crystal system with a centrosymmetric *P*–1 space group. The molecular structure of 4a is shown in Fig. 1, and the crystallographic data and refinement parameters are listed in Table S1 (ESI†). The molecular geometry is defined by characteristic bond lengths, including C11–O2 (1.192 Å), C11–O1 (1.372 Å), C1–O1 (1.446 Å), C2–N1 (1.303 Å), C3–N1 (1.369 Å), and C4–Br1 (1.883 Å). Key bond angles such as O2–C11–O1 (120.3°), C11–O1–C1 (111.53°), C2–N1–C3 (114.80°), C3–C4–Br1 (118.62°), and C5–C4–Br1 (119.59°) are consistent with the expected bonding environment and confirm the structural integrity of the molecule in the solid state.

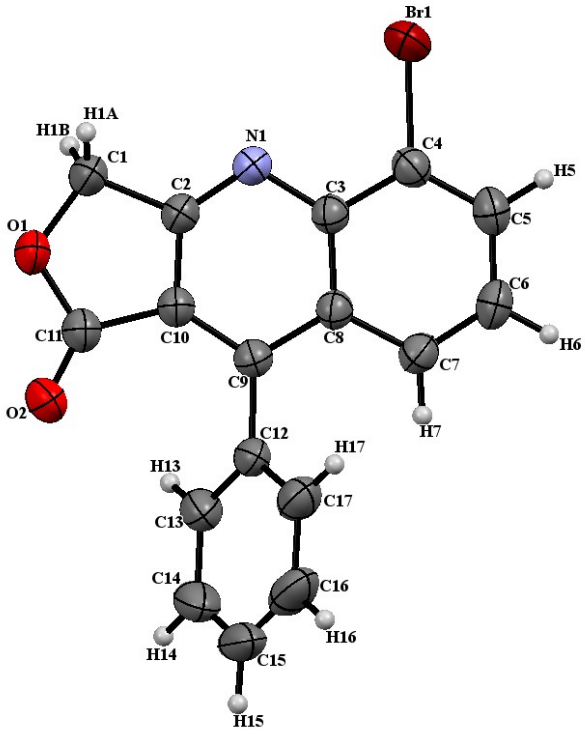


Figure S1: ORTEP diagram of compound **4a** at 50% thermal ellipsoid probability.

Data availability

The crystallographic data for compound **4a** have been deposited with the Cambridge Crystallographic Data Centre (CCDC) under deposition number **2519622** and can be obtained from the CCDC via their website: https://www.ccdc.ac.uk/structures.

Method

X-ray crystallography

Single-crystal X-ray diffraction data were collected on a Rigaku XtaLAB Synergy-I diffractometer using *CrysAlisPro* software, with graphite-monochromated Mo Kα (λ = 0.71073 Å) and Cu Kα (λ = 1.54184 Å) radiation at 293 K. The crystal structures were solved using the SHELXL-97 program implemented in OLEX2.0, and refined by full-matrix least-squares procedures on F^2. Anisotropic displacement parameters were applied to all non-hydrogen atoms.[3,4] Hydrogen atoms were placed in calculated positions and refined using a riding model with idealized geometries. Structural visualization and analysis were carried out using Mercury software for Windows.

Table S1: Crystal data and structure refinement for compound 4a.

Parameters	Compound 4a
CCDC	2519622
Empirical formula	$C_{17}H_{10}BrNO_2$
Formula weight	340.17
Temperature/K	293
Crystal system	Triclinic
Space group	P-1
a/Å	6.94070(10)
b/Å	10.10700(10)
c/Å	10.61130(10)
α/°	79.6910(10)
β/°	77.5300(10)

γ/°	71.1550(10)
Volume/Å^3	683.038(14)
Z	2
ρ_{calc}g/cm^3	1.654
μ/mm^{-1}	4.133
F(000)	340.0
Crystal size/mm^3	0.26 × 0.24 × 0.15
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	8.594 to 136.16
Index ranges	-8 ≤ h ≤ 8, -12 ≤ k ≤ 12, -12 ≤ l ≤ 11
Reflections collected	13242
Independent reflections	2474 [R_{int} = 0.0286, R_{sigma} = 0.0164]
Data/restraints/parameters	2474/0/191
Goodness-of-fit on F^2	1.047
Final R indexes [I>=2σ (I)]	R_1 = 0.0294, wR_2 = 0.0767
Final R indexes [all data]	R_1 = 0.0307, wR_2 = 0.0779
Largest diff. peak/hole / e Å^{-3}	0.40/-0.56

Table S2: Bond Lengths for compound 4a.

Atoms		Length/Å	Atoms		Length/Å
Br^1	C^4	1.883(2)	C^{10}	C^{11}	1.478(3)
O^1	C^{11}	1.372(3)	C^7	C^6	1.362(3)
O^1	C^1	1.446(3)	C^9	C^{12}	1.484(3)
O^2	C^{11}	1.192(3)	C^4	C^5	1.364(3)
N^1	C^3	1.369(3)	C^{12}	C^{17}	1.385(3)

N^1	C^2	1.303(3)	C^{12}	C^{13}	1.395(3)
C^3	C^8	1.431(3)	C^2	C^1	1.493(3)
C^3	C^4	1.417(3)	C^5	C^6	1.396(3)
C^8	C^7	1.418(3)	C^{17}	C^{16}	1.398(4)
C^8	C^9	1.432(3)	C^{13}	C^{14}	1.374(4)
C^{10}	C^9	1.381(3)	C^{16}	C^{15}	1.375(5)
C^{10}	C^2	1.399(3)	C^{14}	C^{15}	1.366(5)

Table S3: Bond Angles for compound 4a.

Atoms			Angle/°	Atoms			Angle/°
C^{11}	O^1	C^1	111.53(17)	C^{17}	C^{12}	C^9	121.7(2)
C^2	N^1	C^3	114.80(18)	C^{17}	C^{12}	C^{13}	119.2(2)
N^1	C^3	C^8	123.63(19)	C^{13}	C^{12}	C^9	119.1(2)
N^1	C^3	C^4	118.44(19)	N^1	C^2	C^{10}	126.86(19)
C^4	C^3	C^8	117.93(19)	N^1	C^2	C^1	124.17(19)
C^3	C^8	C^9	118.79(18)	C^{10}	C^2	C^1	108.96(19)
C^7	C^8	C^3	118.84(19)	O^1	C^{11}	C^{10}	107.77(18)
C^7	C^8	C^9	122.34(19)	O^2	C^{11}	O^1	120.3(2)
C^9	C^{10}	C^2	120.30(19)	O^2	C^{11}	C^{10}	132.0(2)
C^9	C^{10}	C^{11}	132.1(2)	C^4	C^5	C^6	119.6(2)
C^2	C^{10}	C^{11}	107.54(18)	C^7	C^6	C^5	121.4(2)
C^6	C^7	C^8	120.4(2)	C^{12}	C^{17}	C^{16}	119.6(3)
C^8	C^9	C^{12}	122.23(18)	C^{14}	C^{13}	C^{12}	120.2(3)

C^{10}	C^{9}	C^{8}	115.61(19)	O^{1}	C^{1}	C^{2}	104.19(18)
C^{10}	C^{9}	C^{12}	122.16(19)	C^{15}	C^{16}	C^{17}	120.1(3)
C^{3}	C^{4}	Br^{1}	118.62(16)	C^{15}	C^{14}	C^{13}	120.7(3)
C^{5}	C^{4}	Br^{1}	119.59(17)	C^{14}	C^{15}	C^{16}	120.2(3)
C^{5}	C^{4}	C^{3}	121.8(2)				

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